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Hatha Yoga and Arterial Stiffness and Reactivity

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Hatha Yoga and Arterial Stiffness and Reactivity

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Dedication

To my family and friends who loved and supported me throughout this life changing process.

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Hatha Yoga and Arterial Stiffness and Reactivity

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This research assessed the role of Hatha yoga in the modulation of vascular health. In study one, Hatha yoga practitioners were compared to sedentary controls to whom they were matched for age and body mass index. Practitioners of Hatha yoga were no different from sedentary individuals in terms of arterial stiffness or vascular endothelial function. Yoga practitioners possessed lower HbA1c ($P < 0.05$) levels and lower pulse pressure ($P < 0.05$) than their sedentary counterparts. Practitioners of Hatha yoga had lower body fat percentages, but this observed trend did not reach statistical significance ($P = 0.052$). In study two, a 12-week Hatha yoga intervention resulted in reductions in HbA1c levels ($P < 0.05$) and total cholesterol ($P < 0.05$) in previously sedentary adults. No changes were observed in carotid artery compliance or brachial artery flow-mediated dilation as a result of the intervention. In study three, obese and lean, apparently healthy adults completed an 8-week Bikram yoga intervention. Reductions in total- and LDL-cholesterol were observed in the lean subjects ($P < 0.05$), with no changes in lipid profiles in the obese group. The homeostasis model assessment of insulin resistance (HOMA-IR) decreased in the lean subjects, but this trend did not attain statistical significance ($P = 0.06$). Although an observed trend was shown at 60 minutes during the oral glucose tolerance test ($P = 0.07$), glucose tolerance remained unchanged in the obese subjects. Brachial artery flow-mediated improved by approximately 2% in the obese subjects, but this observed change did reach statistical significance ($P = 0.10$). Flexibility increased in both groups as a result of the

Bikram yoga intervention. Therefore Hatha yoga improved lipid profiles and glycemic control in sedentary adults, but no effects on vascular health were demonstrated.

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Chapter I: REVIEW OF RELEVANT LITERATURE

Vascular function provides a gage of cardiovascular disease (CVD) risk, thus providing pertinent information in the assessment of overall cardiovascular health. As CVD is the leading cause of death in the U.S. (105), noninvasive means to assess risk are of vital importance. Both endothelial dysfunction and arterial stiffness can be measured noninvasively, preclude overt CVD, and are independent risk factors for CVD (10, 19). Both arterial stiffness and endothelial dysfunction represent a disruption in vascular homeostasis and impairments in the ability of the vascular endothelium to prevent the development of atherosclerosis and its associated events.

Endothelial Function

Vascular endothelial function is most typically assessed using flow-mediated dilation (FMD) (16). During this procedure, a blood pressure cuff is inflated around the forearm to 100 mm Hg suprasystolic pressure for the duration of 5 minutes. Once the cuff is deflated, reactive hyperemia ensues in order to restore blood flow to the ischemic tissue downstream. Reactive hyperemia elicits a vasomotor response within the brachial artery with the blood flow-induced increase in shear stress along the vessel wall serving as the stimulus for the production of nitric oxide (NO) (26, 74), prostaglandin (40), and endothelial-derived hyperpolarizing factor (EDHF) (4) from the vascular endothelium. Together, these molecular regulators, of which NO being of key importance due to its vasoprotective capacity, elicit vasodilation of the vessel. Thus, FMD provides a means to indirectly determine NO bioavailability.

Nitric oxide is a key molecular regulator of vascular homeostasis stimulated by shear stress and insulin signaling influencing both vascular tone and endothelial function. NO plays a vital role in the prevention of atherosclerosis by inhibiting monocyte chemoattractant peptide-1

(MCP-1) (144, 195), reducing smooth muscle cell proliferation (70, 147, 163), and preventing platelet adhesion (154), all of which are key events in the initiation and progression of atherosclerosis. Thus, any reduction in the NO activity will compromise the ability of the vascular endothelium to perform this vital function, resulting in a shift toward a pro-atherosclerotic state. Accordingly, coronary heart disease and its associated risk factors are all characterized by reductions in NO bioavailablity.

Endothelial dysfunction within the microvasculature is associated with obesity (33) and precedes the onset of hypertension (85, 160). Associations between endothelial dysfunction and blood pressure are presumably explained by increases in total peripheral resistance as a result of an impairment in the ability of the blood vessels to vasodilate (146). Microvascular endothelial function can be assessed using thermal reactive hyperemia (TRH) and post-occlusive hyperemia (PORH). Thermal reactive hyperemia applies thermal provocation to elicit vasodilation within the subcutaneous microvessels via the stimulation of cutaneous thermoreceptors. The blood flow response to local heating occurs in three phases: the initial peak; the nadir; and the plateau. The initial peak is mediated by sensory nerves within the skin while the plateau phase is predominantly influenced by the production of NO (84, 119).

Post-occlusive reactive hyperemia (PORH) involves laser Doppler flowmetry or venous occlusion plethysmography before, during, and after a 5-minute cuff occlusion and is based upon the same concept as FMD in which reactive hyperemia-induced shear stress serves as the stimulus for NO production and subsequent vasodilation within the subcutaneous resistance vessels. This procedure is remains controversial for a few reasons. While TRH is partially dependent upon NO availability (84), PORH is not altered in the absence of this key molecular regulator (188) nor is it enhanced by increased bioactive levels of NO (197). Endothelial-derived hyperpolarizing factor influences endothelium-dependent vasodilation to a greater extent in small, resistance than in larger conduit arteries (169) and may thus facilitate PORH in the absence of NO in these investigations. Additionally, unlike TRH (111), prostanoids have been implicated in PORH (101). Moreover, previous investigations have failed to find correlations between this measure and the more traditional index of endothelial function and NO availability, FMD (36, 193). Despite previous indications of its lack of clinical relevance, PORH has been shown to be related to Framingham risk scores (178) and, like NO-dependent responses, is also impaired in diabetic patients compared with healthy controls (168).

Aerobic exercise improves endothelial function in healthy and patient populations via increases in NO bioavailability (34, 62). During exercise, cardiac output is increased in proportion to the intensity of the activity. The elevation in cardiac output during exercise serves as a stimulus for NO production as it results in increases in shear stress along the arterial walls. It is believed that the exercise-induced improvements in endothelial function are mediated in part by shear stress. This hypothesis is supported by the experiment based on the functional adaptations to repeated bouts of warm water immersion (54). While both arms were submerged in warm water, one arm was occluded in order to prevent the increase in blood flow in response to the heat stress. Improvements in microvascular function as indicated by TRH were evident after 4 weeks and these alterations were limited to the non-occluded arm. No changes in endothelial function in the occluded arm were displayed. These results support the notion that repeated elevations in shear stress can account for both the exercise and thermal therapy-induced increases in microvascular vasodilator function.

Arterial Stiffness

Pulse wave velocity (PWV) and simultaneous ultrasonography and tonometric blood pressure analysis (arterial compliance) are two common methods by which arterial stiffness can be quantified. Pulse wave velocity involves the measurement of the velocity of a pressure wave that is initiated at the left ventricle upon contraction and travels toward the periphery. Arterial compliance involves simultaneous ultrasound imaging and blood pressure waveform analysis and provides information regarding the ability of the vessel to expand and recoil for a given pulse pressure. Both arterial compliance (61) and arterial stiffness (10) provide prognostic value independent of the Framingham risk score and are mediated by both compositional and functional changes within the vessel wall that occur with age and in the presence of certain disease states. Thus, the two terms are often used interchangeably.

Functional properties that affect arterial stiffness are sympathetic-adrenergic vasoconstrictor tone exerted on vascular smooth muscle cells (9, 53, 108) and the production of vasoactive regulators like NO (93, 94, 113, 159, 186), endothelin-1 (106), and angiotensin II (99, 166). Compositional changes within the vessel wall such as decreases in elastin and increases in collagen deposition also contribute to arterial stiffness (126). Of the factors influencing arterial stiffness, compositional wall properties are more resistant to aerobic exercise-induced adaptations (126) while functional properties such as NO availability and endothelin-1 concentrations are more adaptable. The mechanisms by which central arterial stiffness can be attenuated with aerobic exercise in healthy and in patient populations (24, 68, 161, 162) include reductions in sympathetic nervous system activation and ET-1 activity, increases in NO availability due, in part, to reductions in inflammation and oxidative stress (6, 145, 159).

Peripheral arterial stiffness, which is linked less to CVD, can be measured via femoral or popliteal arterial compliance or femoral-ankle pulse wave velocity. Unlike the central arteries, the elastic properties of the peripheral arteries are more resistant to exercise-induced or age-related adaptations (25, 68, 161). A potential explanation for the discrepancies between central and peripheral arteries are that the femoral arteries do not play a key role in the buffering of cardiac pulsations and that the magnitude of distension and recoil in response to a given cardiac cycle is much less than that of the aorta. Despite most of the previous results regarding this measure, one investigation found an exercise-induced increase in peripheral arterial compliance in response to sprint interval training (137). However, given that most previous data are contrary to this finding, it is generally believed that the peripheral arteries do not stiffen with age, nor are they amenable to exercise-induced adaptations.

Obesity and Vascular Function

Obesity is a CVD risk factor affecting over one third of the U.S. population (45) contributing to the development of atherosclerosis in part through its effects on endothelial function and arterial stiffness (39). Obesity is associated with chronic, low-grade inflammation (67), impaired insulin signaling (100, 158), and elevations in sympathetic nervous system activation (100, 148), each of which could serve as mechanistic links between obesity and vascular dysfunction. Inflammation, as indicated by elevations in inflammatory cytokines, is associated with increased cardiovascular risk (142, 152), presumably through its effects on the vasculature (176). Acute inflammation induced via Salmonella typhi vaccination has been shown to cause endothelial dysfunction in aortic cells (71, 86, 179) as well as elevations in arterial stiffness (176, 179). The mechanism by which inflammation impairs vascular function is through elevations in superoxide anions, which react with NO to form peroxynitrite resulting in a reduction in the bioavailability of NO (134, 196).

Obesity is associated with elevations in inflammatory markers, C-reactive protein, TNFα, interleukin 6 (IL-6) and IL-8. Macrophages within adipose tissue secrete inflammatory cytokines IL-6, IL-8, and TNFα (67), of which TNFα is thought to be of key importance. The induction of TNFα in undifferentiated preadipocytes results in an increase in the levels of IL-6, IL-8, and MCP-1 whereas the inhibition of this cytokine has been shown to preclude the inflammatory process in cultured cells and in patients with inflammatory diseases (1, 98). These findings are indicative of a regulatory role of this cytokine in the inflammatory process. TNFα has also been linked to endothelial dysfunction (196) and impaired insulin-stimulated NO production (91).

C-reactive protein (CRP) is an inflammatory marker known to increase CVD risk (83, 104, 141-143) and is elevated in obese individuals (39, 46, 175). C-reactive protein is also associated with arterial stiffness (192) and endothelial dysfunction (170) and is thus thought to play a role in the progression of atherosclerosis. CRP facilitates the atherogenic and inflammatory processes by activating stress-activated protein kinases p38 and C-jun terminal kinase (JNK) (66, 134), elevating reactive oxygen species (ROS) formation from inducible or iNOS overproduction of NO (180), increasing adhesion molecule formation (130), increasing endothelin-1 production(172), and decreasing NO bioavailability (174). The role of CRP in activating C-jun terminal kinase may also explain the link between inflammation and insulin resistance and this stress kinase impairs cellular insulin signaling (131, 135).

Interleukin-6 and IL-8 are inflammatory cytokines secreted from adipose tissue that also play a role in facilitating the progression of atherosclerosis. Interleukin-6 has been shown to stimulate the production of C-reactive protein and increase the expression of adhesion molecules within the vascular endothelium (189). When infused chronically, IL-6 increases oxidative stress and impairs endothelium dependent vasodilation in aortic tissue extracted from mice (182). The effects of IL-6 on vascular endothelium could account for the relationship between IL-6 and blood pressure in healthy, normotensive men and women (5, 17). In addition, the hypertensive response to the infusion of angiotensin II, a potent vasoconstrictor released from adipose tissue, is attenuated in IL-6 knockout mice further suggesting a role of this cytokine in the regulation of blood pressure (102).

Resistin is an adipokine secreted from adipose tissue that has been implicated in the inflammatory process and may contribute to insulin resistance by reducing GLUT-4 expression (43, 158). Resistin increases the production of inflammatory cytokines via nuclear factor kappa B (NFκB) signaling (149), adhesion molecules in endothelial cells (21, 173), and stimulates smooth muscle cell proliferation and migration. This adipokine also facilitates endothelial dysfunction by reducing eNOS mRNA expression and NO bioavailability and upregulating ROS production (20).

Insulin resistance is an underlying pathology associated with obesity in which post membrane insulin signaling is diminished. Elevations in TNFα associated with obesity impair insulin signaling by activating stress kinases, of which c-Jun terminal kinase (JNK) is the primary culprit (183). JNK is a mitogen activated protein kinase (MAPK) that is activated by endoplasmic reticulum stress, elevated fatty acid levels, reactive oxygen species, and inflammatory cytokines, each of which is associated with obesity (82, 155, 183). JNK is not only activated by inflammation, but also, once activated, promotes further inflammation by stimulating the transcription of inflammatory genes within the cell nucleus. This stress kinase contributes to insulin resistance by phosphorylating serine residues of IRS-1 and thus, preventing the phosphorylation of IRS-1 by tyrosine in response to the binding of insulin to its membrane receptor (131, 135). This inhibition of IRS-1 phosphorylation precludes downstream insulin signaling and impairs insulin action.

Insulin resistance contributes to vascular dysfunction through a decline in insulin-stimulated eNOS activation and thus NO production from L-arginine within the vascular endothelium (92, 123). The activation of AKt in response to the phosphorylation of IRS-1 results in the activation of eNOS. Thus, the effects of insulin are not limited to the metabolic needs of the cells, but encompass the vasculature by facilitating vasodilation and end-organ blood flow. Insulin resistance results not only in a reduction in insulin-stimulated glucose uptake, but also endothelial dysfunction brought on by a reduction in NO production from the vascular endothelium.

Hyperinsulinemia is associated with insulin resistance and represents an attempt at overcompensation for the impairment in insulin action. Insulin activation of MAPK within the cell results in the production of ET-1, which is the molecular antagonist of NO (92, 123). This pathway is independent of the IRS-1 signaling pathway and is not adversely affected by impairments in insulin action. Endothelin-1 is a vasoconstrictor that contributes to arterial stiffness with age. The hyperinsulinemic response to insulin resistance promotes the activation of this vasoconstrictor in the absence of insulin-stimulated NO production resulting in a shift within the vessel toward a proconstrictive and proatherosclerotic state.

The homeostasis model assessment (HOMA-IR) (109) is often used to estimate insulin sensitivity and is based on fasting insulin levels. A cut-off value of 3.22 is used for adults with higher HOMA-IR scores being indicative of insulin resistance. A range of 2.5 to 3 has also been used in order to distinguish insulin sensitive from insulin resistance subjects (107). Elevated

HOMA-IR values are associated with cardiac and cerebrovascular events and CRP levels (12), further supporting the link between insulin resistance and vascular dysfunction.

Hatha Yoga

Hatha yoga is an ancient tradition involving meditation, breathing exercises (pranayama) and postures (asanas), which has emerged as a popular mode of exercise in the U.S. over the past 50 years. Yoga originated as a means to achieve perfection and happiness and involved the practice of morality and contentment. With its transition from Eastern to Western cultures, it has become primarily a means by which to reduce stress and improve physical fitness. Among the many forms of Hatha yoga are Hatha flow, Vinyasa, Ashtanga, Kundalini, and Bikram.

Hemodynamic and Metabolic Responses to Hatha Yoga

Unlike most exercise modes, yoga is a hybrid form of physical activity which consists of isometric contractions, static stretching, breathing exercises, and meditation. Few studies have attempted to determine the metabolic cost of this activity compared with more traditional forms of aerobic exercise. Most studies have demonstrated that the average intensity of yoga is within the mild to moderate intensity range based on percentage of maximal heart rate and oxygen consumption (VO_2) (7, 22, 31, 37, 60). The average intensity of a Hatha yoga session has ranged from 14.5% (22) to 34% (37) maximal oxygen consumption (VO_2max) approximately 2 METs (22, 60).

It should be noted that a typical yoga session consists of postures held for 30 seconds to one minute with frequent breaks in between consisting of lying in the supine position. Therefore, when the intensity across the entire session is averaged, it includes the intensity of these frequent breaks in between postures called savasanas or corpse poses. There is a vast difference in intensity between some of the yoga postures versus corpse pose. For instance, Warrior III (APPENDIX A) elicits a VO_2 of 14.6 mL/kg/min or 4 METs and a heart rate equivalent to 72% of max while corpse pose (APPENDIX D) or the break in between postures results in a VO_2 of 3.6 mL/kg/min or 1 MET and is equivalent to 40% of maximum heart rate (7).

The intensity of Hatha yoga was found to be lower than treadmill walking at 3.5 mph at approximately 57% of maximum heart rate (MHR) (22). This investigation also demonstrated the variability between various postures in that the sun salutation series resulted in an average heart rate equivalent to 67% MHR while all other postures resulted in an average of 56% MHR. The sun salutation is a continuous flow of standing and floor postures that is generally included as a warm up and performed for 5 minutes. This results in an initial rise followed by a sustained increase in heart rate and VO_2, while all other postures are performed intermittently with savasanas dispersed in between. Therefore, on average, both heart rate and VO_2 responses are higher on average during the sun salutation than during all other postures.

Blood pressure responses to yoga poses have also been shown to vary substantially with blood pressure responses to Warrior III of 165 and 100 mmHg, to bridge pose of 121 and 77 mmHg, and to corpse pose of 113 and 70 mmHg for systolic and diastolic, respectively (7). On average, positions in which the back is arched induce the greatest increases in systolic, diastolic, and mean blood pressures. Previous data collected in our laboratory in which blood pressure and heart rate were measured continuously throughout a series of yoga postures using beat-by-beat finger plethysmography support these findings demonstrating that the systolic blood pressure and heart rate responses to postures performed in the seated and lying positions are not different from baseline while most other standing postures result in increases in these measures (Miles et al.

unpublished observation Appendices B & C). These data also show that most yoga postures result in increases in heart rate, stroke volume, and cardiac output (Appendix C).

Hatha Yoga and Blood Pressure

The efficacy of Hatha yoga in reducing blood pressure has been demonstrated in healthy and in patient populations. Vinyasa is a style of Hatha yoga employing a continuous progression of postures with simultaneous breathing exercises. This form of yoga is also known as “power yoga” due to the more vigorous nature of this style of Hatha yoga. Vinyasa yoga resulted in reductions in body mass, systolic blood pressure, insulin concentrations, and triglycerides in individuals with at least one metabolic syndrome risk factor when performed twice per week for a 3-month period (191). Another more traditional form of Hatha yoga, Iyengar yoga, has also been shown to reduce 24-hour blood pressures in pre-hypertensive and stage-I hypertensive individuals (23). These findings have been replicated in healthy and in patient populations (13, 110, 151). While most studies have shown reductions in blood pressure after an 8-12 week period, a time course of change in blood pressure has been investigated with findings of systolic and diastolic blood pressure reductions after two weeks of performing yoga postures three times per week with a more progressive steady decline over the next 6 weeks (110).

Hypotensive effects of yoga may be explained in part by the isometric muscle contractions involved during most yoga postures as isometric exercise training reduces blood pressures in hypertensive patients (164) and normotensive adults (35, 138, 185). Recent findings suggest that reductions in systolic, diastolic, and mean blood pressures with isometric training can be seen in as little as 4 weeks (35). There is some variability in the type of isometric exercises performed in these studies in that most have employed handgrip exercises, while others have used lower body isometric contractions. Most yoga postures involve isometric contractions of the leg muscles, while few inverted postures consist of arm isometric contractions. Although both handgrip and lower body isometric contractions have been effective in reducing blood pressures, the results concerning isometric handgrip muscle contractions and endothelial function have been inconsistent with some showing improvements in FMD (44, 117) while others show no change in this parameter in normotensive individuals (114). Therefore, it is currently unclear whether the reduction in blood pressure with isometric training is due to improvements in endothelial function.

Yoga and Vascular Function

Empirical data indicative of the impact of yoga on the vasculature are scarce. One investigation seeking to unveil the effects of yoga on endothelial function in patients with coronary artery disease (CAD) implemented a 6-week Hatha yoga intervention in patients and in healthy subjects (151). A 69% nonsignificant improvement in endothelium-dependent dilation was demonstrated in CAD patients while no changes in this measure occurred in healthy individuals. Endothelium-independent dilation did not change as a result of the intervention.

Arterial stiffness has been shown to be lower in yoga practitioners than in sedentary individuals as measured by pulse wave velocity and carotid arterial compliance (41). Both measures of arterial stiffness were not different from those obtained from aerobically trained individuals, suggesting that although the intensity of yoga does not match that of moderate to vigorous aerobic exercise, similar effects on vascular health may still be obtained. An additional finding of this study was that systolic blood pressure was lower in practitioners of yoga than in aerobically-trained individuals, which reinforces a hypotensive effect of yoga.

Hatha Yoga and Inflammation

Although the effects of yoga on inflammation have not been studied extensively, two investigations have attempted to elucidate the role of yoga in mediating the inflammatory response. An 8-week Hatha yoga intervention consisting of 3, 70-minute sessions per week reduced IL-6 and CRP levels and increased extracellular superoxide dismutase in chronic heart failure patients (132). A similar intervention conducted in a predominantly African-American sample of heart failure patients consisting of an 8- to 10-week Hatha yoga intervention resulted in a reduction in IL-6 and CRP levels and an increase in superoxide dismutase (133). Consistent with previous findings, it has also demonstrated that advanced practitioners of hatha yoga have reduced baseline IL-6 levels and produce less LPS-stimulated IL-6 in response to emotional and physiological stressors when compared with novice practitioners (88).

Hatha Yoga and Glucose Metabolism

The role of yoga in mediating glucose metabolism has not been well established. Although it has been found to reduce fasting glucose concentrations and HbA1c in individuals with facets of the metabolic syndrome (87), the yoga intervention implemented in this investigation was combined with usual patient care, which was not described by the authors and could have accounted for the changes seen in these factors. Hatha yoga has also reduced fasting blood glucose levels in diabetic patients (52). Additional findings from this investigation include reductions in total cholesterol and lipid peroxidation and increases in superoxide dismutase levels further indicating a role of yoga in mediating CVD risk profile.

Perhaps the effect of yoga on blood glucose levels is driven by the isometric or stretching components of the postures as both have been shown to improve glycemic control (18, 38, 75, 80). Passive stretching of skeletal muscle increases glucose uptake (75) via Akt and p38 mitogen-activated protein kinase (MAPK) (80) and reactive oxygen species signaling independent of PI3-K (18). The increase in glucose uptake that accompanies passive stretching occurs independently of changes in the energy state of the cell as reflected by ATP, ADP and AMP levels, or AMP activated protein kinase. Thus, it appears that stretching mimics both aerobic and strength training in serving as a stimulus for the translocation of GLUT4 to the cell membrane and facilitating glucose uptake. The activation of this signaling cascade could improve post membrane cellular signaling in response to insulin and thus result in improvements in insulin action.

Flexibility and Arterial Stiffness

Flexibility is a major component of yoga practice as several of the postures include static stretching and are aimed at improving joint range of motion. Our laboratory has previously shown that 13 weeks of intense stretching performed 3 days per week for 30 to 45 minutes per day elicited improvements in carotid arterial compliance (29). In addition, a negative correlation has been found between trunk flexibility and arterial stiffness in older individuals, with a lack of relationship demonstrated in young adults (190). Decreases in elastin content and increases in collagen cross linking within the vessel walls occur with age and contribute to the loss of arterial distensibility. These structural changes also occur within skeletal muscle, and contribute to the age-related loss of joint range of motion. The similarities in adaptations with age can partially explain the relationship seen between vascular and skeletal muscle properties in older individuals. These findings suggest the possibility that yoga, which has been associated with improvements in flexibility (133), may improve arterial distensibility.

Resistance Training and Arterial Stiffness

Isometric strength training is another primary component of yoga postures that could affect arterial stiffness. Several previous studies have shown increases in arterial stiffness with strength training (30, 120, 127, 128) while others have found no changes in this vascular parameter (14, 15, 136, 194). The proposed mechanism by which arterial stiffness increases with resistance training is the substantial increase in blood pressures that occur during the strength training exercises. Yoga postures are associated with increases in blood pressures that mimic that of strength training. Data from our laboratory show that among yoga practitioners, systolic and diastolic blood pressures increase up to ~190 mmHg and ~90 mmHg during some of the standing yoga postures. These increases in blood pressure that occur during the postures may counteract the beneficial effect of stretching on arterial compliance.

Yoga, Stress and Anxiety

Meditation is a key component of yoga practice that is employed throughout some classes as in Bikram yoga and dispersed intermittently throughout others that may exert effects on mental health. Accordingly, yoga has been associated with reductions in stress, anxiety, depression, and fatigue along with improvements in physical wellbeing, vigor, and mental health (110, 118, 153, 184). Mental stress increases cardiovascular risk (56, 79) in part through impairments in insulin action (121) and vascular dysfunction (11, 48, 156), and increasing platelet aggregation (57). Thus, a potential role of yoga in improving cardiovascular risk profile could be mediated by the impact of this mode of exercise on lowering mental stress and improving mental health.

Bikram Yoga

Bikram yoga is a trademarked form of hatha yoga in which a standard series of 26 postures (APPENDIX D) is performed in a room heated to 105°F with 60% relative humidity. During each class, the instructors follow a script to instruct and encourage each practitioner throughout the 90-minute class. This form of yoga lends itself to study due to the heavily controlled conditions. There are approximately 300 Bikram yoga studios operating in the U.S. with several hundred more worldwide. Bikram yoga is rapidly growing in popularity despite the lack of evidence supportive of its associated health benefits.

Bikram yoga has been shown to improve knee extensor strength and standing balance time in healthy young adults when performed consistently for 8 weeks (65). These improvements were anticipated as several of the postures are performed while standing on one leg and are aimed at improving balance. Practitioners of Bikram yoga have also possessed bone mineral density values that are above average based on their age- and ethnicity-based norms (122). These findings suggest that this mode of yoga is an effective means by which to improve balance, a benefit which could be maximized in elderly individuals in whom balance time is reduced.

Although the benefits of this form of yoga have not been elucidated, it can be hypothesized that the health benefits of other forms of Hatha yoga would also be present in practitioners of Bikram yoga. The unique feature of Bikram yoga that separates it from other forms of Hatha yoga is the temperature at which it is performed. The heat and humidity employed during Bikram yoga mimic that of a sauna and the thermal component alone could serve as a stimulus for added benefits.

Thermal Therapy and Vascular Function

Warm water immersion elicits increases in heart rate, cardiac output and oxygen consumption (8, 165). Thus, subjection to hyperthermic conditions induces cardiovascular and metabolic responses similar to those induced via aerobic exercise. The increase in cardiac output may facilitate improvements in macro- and micro-vessel endothelial function. In patients with chronic heart failure, sauna therapy improves endothelium dependent dilation (90). Other hemodynamic improvements included reductions in systolic blood pressure, cardiothoracic ratio, and left ventricular end diastolic diameter. The improvements in endothelial function occurred in the absence of changes in inflammation or oxidative stress. Thus, the investigators concluded that the improvements in endothelial function were mediated by the thermal provocation induced increases in shear stress.

Sauna therapy has also been shown to augment endothelium dependent dilation in men with coronary risk factors (78). These improvements were accompanied by declines in systolic and diastolic blood pressures, and fasting plasma glucose levels. Similar to previous findings, these changes occurred independent of alterations in oxidative stress. Thus, the investigators again concluded that the improvements in endothelial function were mediated by increases in eNOS production of NO after repeated intermittent increases shear stress.

Thermal Therapy and Glycemic Control

Thermal therapy also mimics aerobic exercise in improving glycemic control and insulin action. Hot-tub therapy has resulted in reductions in blood glucose levels and improvements in glycosylated hemoglobin in patients with type 2 diabetes (73). One study attempted to elucidate a mechanism facilitating these alterations with thermal therapy employing a similar intervention in an animal model while subjecting the animals to high-fat feeding. Water submersion resulting in an increase in core temperature from 36 to 41.5°C for 20 minutes once per week for 12 weeks was the mode of thermal therapy utilized in this investigation. High-fat feeding is a frequently used model of inducing insulin resistance in animals (63, 81, 129). Thermal therapy resulted in an attenuation of high-fat feeding-induced hyperinsulinemia and glucose intolerance in the high-fat fed animals (58). Heat shock protein (HSP)-72, -25, and mitochondrial HSP-60 also increased as a result of the thermal therapy, of which, HSP-72 and -25 were proposed as the primary facilitators of the improvements in insulin signaling.

Heat shock proteins have been shown to prevent the activation of stress kinase, JNK (59, 103), and may prevent the inhibition of insulin mediated tyrosine phosphorylation of IRS-1 and insulin resistance. In support of previous findings of an inhibitory role of heat shock proteins on stress kinase activation, heat treatment resulted in reductions in JNK and IKK-β activation in this investigation (58). To further investigation a role of thermal therapy in mediating glucose uptake, insulin stimulated 2-deoxy glucose uptake was measured after a single bout of heat treatment and found to be significantly increased in the extensor digitalis longus. Thus, it appears that thermal therapy in the absence of exercise promotes insulin signaling by suppressing the phosphorylation of IRS-1 by stress kinase competitors.

Whole body hyperthermia has been shown to induce transient increases in GLUT-4 translocation and blood glucose levels, improved glucose tolerance, and reduced insulin levels in obese animals with type 2 diabetes (96). In addition, a more recent investigation has shown that hot-tub therapy increased insulin secretion, antioxidant levels, and HSP-70 levels and reduced lipid levels and the formation of advanced glycated end products in diabetic animals (3). Moreover, thermal therapy has attenuated the reduction in fat oxidation in cells chronically exposed to palmitate, which was supported by an additional finding of a reduced fat pad weight in these animals (58). These results lend support to previous findings indicative of the efficacy of thermal therapy in improving both glucose and fat metabolism.

Collectively, results from previous investigations indicate that yoga may reduce blood pressure and promote vascular health in obese individuals, possibly due to reductions in inflammation. In addition, the association between flexibility and arterial stiffness suggests that yoga may reduce arterial stiffness. Based on previous findings indicative of the effectiveness of thermal therapy in improving glycemic control and vascular function, it is plausible that Bikram yoga would improve these variables in obese individuals in whom both vascular function and glycemic control are likely impaired.

Chapter 2: Study 1: Advanced Yoga Practitioners versus Sedentary

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in the U.S. and coronary artery disease accounts for over half of the CVD-related deaths annually (105). Obesity is CVD risk factor associated with arterial stiffening (32, 124, 140) and endothelial dysfunction (39, 157), both of which have been implicated in the progression of coronary artery disease and cardiac events (10, 19, 51, 139, 150). Obesity is characterized by low grade inflammation (67) and elevations in adrenergic stimulation (100, 148), and is associated with impairments in insulin action (158), each of which could provide a link between obesity, vascular dysfunction, and CVD. Given that obesity currently affects over one third of adults in the U.S.(45), interventions aimed at reducing prevalence rates and treating its associated pathologies are of paramount public health importance.

Yoga has been rapidly gaining popularity in the U.S. as a means of enhancing general health. Hatha yoga is the most commonly practiced form of yoga in the U.S. and consists of pranayama (breathing), meditation, and strengthening, balancing and flexibility-enhancing asanas (postures). Hatha yoga serves as a basis for many forms of yoga, including Vinyasa, Ashtanga, Iyengar, and Bikram yoga, each of which is performed in a standardized fashion. Although research findings indicative of a role of yoga in improving physical and mental health are accumulating, little is known of its role in the prevention of CVD or its effects on vascular function.

Yoga postures primarily consist of static stretching and isometric exercises. While the effects of stretching on endothelial function remain indefinite, it has been previously shown that

12 weeks of intense stretching improves carotid arterial compliance, a key factor in the development of CVD (29). Moreover, an inverse association between trunk flexibility and pulse wave velocity, an index of arterial stiffness, has been reported (190). Isometric exercise training elicits reductions in blood pressure in healthy and hypertensive populations (35, 138, 164, 185) as well as augmentations in endothelial function (44, 117). Collectively, these studies indicate that interventions aimed at improving flexibility and isometric strength may positively impact central arterial stiffness and endothelial function and thereby reduce the risk of coronary heart disease. Given that yoga consists primarily of these two components, it is plausible that yoga may elicit improvements in these key vascular functions. However, this hypothesis has not been examined.

Accordingly, the general aim of the dissertation study is to determine the role of yoga in improving vascular function as well as insulin resistance. In order to address this aim as comprehensively as possible, we propose to perform 3 different but related studies. Study #1 is a cross-sectional study that will determine whether advanced practitioners of Hatha yoga will demonstrate a greater arterial compliance and endothelial function compared with sedentary individuals. Study #2 is an intervention study design that will assess the effectiveness of Hatha yoga in improving arterial compliance and endothelial function in previously sedentary adults. Study #3 is another intervention study that will establish the efficacy of Bikram yoga in improving endothelial function and glucose tolerance in obese and lean individuals.

SPECIFIC AIMS

The primary aims of the dissertation study are to determine: 1) whether regular yoga practitioners display greater central arterial compliance and endothelial function than sedentary individuals using a cross-sectional study design; 2) if Hatha yoga will improve arterial compliance and endothelial function in previously sedentary individuals; and 3) the efficacy of Bikram yoga in improving endothelial function, arterial compliance, and glucose tolerance in obese individuals to a greater extent than in lean, apparently healthy adults.

HYPOTHESES:

1) Advanced yoga practitioners will exhibit greater arterial compliance than sedentary individuals.

2) Advanced yoga practitioners will demonstrate enhanced endothelial function as measured by FMD than sedentary adults.

SUBJECTS

Apparently healthy, sedentary adults and advanced yoga practitioners were recruited from the Austin area to serve as subjects for this investigation. Advanced yoga practitioners must have practiced yoga at least three times per week consistently for the past year, and sedentary individuals must have been sedentary for the 6 months prior to this study. All procedures were approved by the Institutional Review Board at The University of Texas at Austin.

EXPERIMENTAL DESIGN

The two groups (sedentary and yoga practitioners) were compared in carotid arterial compliance and brachial artery FMD. One-way ANOVA was used to assess group differences.

Data and Instrumentation

Subjects were required to fast for at least 12 hours in order to obtain fasting plasma lipids and glucose levels. Additionally, fasting was required for the vascular function measures in order to avert the effects of meal content and the hormonal response to food ingestion on vascular function (50, 55, 177).

1) **Research Health Questionnaires** (Appendix E) were completed prior to the session in order to obtain information about general health, family history of disease and physical activity levels. Exclusion criteria include: i) pregnancy; ii) smoking within the past six months; iii) uncontrolled hypertension-defined as blood pressure >140/90 mmHg while on antihypertensive medication; iv) personal history of diabetes or fasting blood glucose >126 mg/dL, heart disease, or other cardiovascular problems; v) barium test within two weeks prior; vi) recent nuclear medicine scan or injection with and x-ray dye within one week prior; or vii) infection in the last four weeks.
2) **Body composition** was estimated non-invasively via dual-energy X-ray absorptiometry (DEXA) using a Lunar Dual Energy X-Ray Absorptiometry DPX (General Electric Medical Systems, Fairfield, Connecticut). This procedure required that the subject lay down on a padded table that emits energy for approximately five minutes while an arm passed overhead and involves a small amount of radiation which is equivalent to less than 1/20 of a chest X-ray.

   Blood samples consisting of 1 ethylenediaminetetraacetic acid (EDTA) and 1 serum tube (~ 6 teaspoons) were obtained by venapuncture using a Luer-lok access device (Becton Dickinson Medical, Franklin Lakes, NJ) and were analyzed for total (TC)-, HDL- and LDL-cholesterol, triglyceride, glucose levels and glycosylated hemoglobin (HbA1C). In addition, a 500-μL whole blood sample taken from an EDTA tube were analyzed for blood viscosity, which were used in the calculation of shear stress, using a DV-I+ viscometer with a CPE-40 cone spindle (Brookfield Engineering Laboratories, Inc., Middleboro, Massachusetts). The Cholestech-LDX system (Cholestech Corp., Hayward, CA) were used to measure total- and HDL-cholesterol, triglyceride and glucose levels using reflectance photometry. For this procedure, a 35 μL blood sample was applied to the test cassette sampling well and once the test was initiated, the color changes of the TC and HDL cholesterol, triglyceride, and glucose reagent pads located within the device were converted to concentration values. LDL-cholesterol were calculated using the Friedewald (47) equation: LDL-C = TC – HDL-C – (TRG/5)

This equation is only valid when triglyceride levels are below 400 mg/dL.

A 10-μL whole blood sample were used to obtain HbA1C, which is a measure of glycosylated hemoglobin and an index of glycemic control over time that has been shown to correlate with cardiac events (27). Glycosylated hemoglobin (HbA1c) were tested via affinity chromatography, a procedure which involved protein separation based on protein-ligand interactions, using the BIO RAD Micromat II (BIO RAD, Hercules, CA).

3) **Carotid arterial compliance** was measured noninvasively via simultaneous acquisition of ultrasonographic arterial diameter images and arterial pressure waveforms. All vascular measures were taken in a temperature-controlled environment to reduce the effect of environmental temperature on vascular measures (42) and in the morning to avoid diurnal changes these variables (97). Brachial systolic (SBP) and diastolic (DBP) blood pressures were measured in the supine position using the STBP (Colin Medical Instruments, San Antonio, TX) and mean arterial pressure (MAP) and pulse pressure (PP) were calculated. Premenopausal female subjects were tested during the early follicular phase of the menstrual cycle in order to control for the effects of estrogen and progesterone on vascular function. Estrogen and progesterone increase eNOS activity (69) which results in augmentations in both arterial compliance (49) and FMD (187).

Arterial compliance was measured after the subject had rested in the supine position for at least 15 minutes. The iE33 ultrasound machine (Philips Medical Systems, Bothel, Washington) equipped with a high-resolution linear array transducer was used to obtain longitudinal images of both arteries 1-2 cm proximal to the carotid and femoral bifurcation sites. Beat-by-beat blood pressure waveforms were obtained via applanation tonometry from the contralateral artery using the VP 2000 (Colin Medical Instruments, San Antonio, Texas) for the carotid and the Colin Pilot for the radial artery. The simultaneous measurement of arterial diameter and pressure alterations throughout a series of at least 10 cardiac cycles permit the non-invasive determination of arterial compliance.

Carotid arterial compliance values were calculated variables using blood pressure waveforms obtained from the contralateral carotid and radial arteries. Carotid blood pressures were calibrated by equating DBP and MAP to brachial DBP and MAP in order to minimize the effect of peripheral impedance on systolic blood pressure. Carotid and radial blood pressure waveforms were calibrated using the following equation:

$$[(MAP_{peripheral} - DBP_{peripheral})/(MAP_{central} - DBP_{central})]*PP_{central} + DBP_{peripheral} = SBP_{carotid}$$

Ultrasound images were analyzed for changes in arterial diameter using Carotid analyzer software (Medical Imaging Applications, Coralville, IA). Carotid artery compliance was calculated by dividing the change in arterial diameter (D) by carotid pulse pressure in the following equation:

$$\Pi(D_{Systolic}^2 - D_{Diastolic}^2)/4PP = \text{Arterial compliance}$$

In addition, β-stiffness index (72), an index of arterial stiffness that adjusts for the effect of alterations in distending pressure on arterial diameter in the following equation:

$$\log(SBP_{carotid}/DBP_{carotid})/[(D_{systolic} - D_{diastolic})/D_{diastolic}]$$

4) **Endothelium-dependent vasodilatory function** was measured noninvasively using brachial artery flow-mediated dilation (FMD) (16, 28). Brachial artery FMD was measured while the subject rested in the supine position in a quiet, temperature-controlled room. A blood pressure cuff was placed around the subject's forearm and subsequently inflated using the E20 Rapid Cuff Inflator, AG101 Air Source, and Rapid Version Cuffs, (D. E. Hokanson, Bellevue, Washington) for five minutes to 100 mmHg above systolic blood pressure. Brachial artery images and blood flow velocity were obtained using the iE33 Doppler ultrasound machine (Philips Medical, Bothel, Washington). A longitudinal image of the brachial artery was acquired 5 to 10 centimeters proximal to the antecubital fossa. Baseline ultrasound images of the brachial artery were obtained prior to cuff inflation and 1-minute post deflation. All brachial artery images were analyzed for diameter changes using the Brachial Analyzer Software (Vascular Tools Version 5, Medical Imaging Applications, Coralville, Iowa) and FMD was calculated as the percent change from an average of 10 baseline diastolic diameters and the average of three maximal systolic diameters.

RESULTS

A total of 51 subjects (28 sedentary and 23 yoga practitioners) were recruited for the current study. In order to isolate the effect of hatha yoga on key outcome variables as much as possible, those who engaged in aerobic exercise training more than two days per week were excluded. Only those who have practiced yoga at least 3 days per week for the past year were included in the practitioner group.

The preliminary data indicated that significant differences in body mass and BMI existed between the two groups. In order to eliminate the potential confounding effect of body fatness, the groups were further matched for BMI values. After all exclusions were made, a total of 34 subjects (18 sedentary and 16 practitioners) were included in the analyses. Two of the sedentary subjects and 4 of the yoga practitioners were males.

Selected subject characteristics are presented in Tables 1 and 2. No group differences were found in any anthropometric or hemodynamic characteristics. Although not statistically significant, a trend towards lower body fat percentage among yoga practitioners was observed ($P=0.08$). Blood lipids and glucose were not different between groups. Yoga practitioners had lower HbA1c than sedentary adults ($P<0.05$). Sleep quality scores were lower among yoga practitioners, indicating better sleep quality than their sedentary counterparts.

Despite the lower carotid pulse pressure among yoga practitioners, the groups were not different in terms of carotid artery compliance as shown in Figure 1 ($P=0.21$). There were also no group differences in β-stiffness index as shown in Figure 2. There were no group differences in brachial artery FMD or baseline artery diameters between the two groups as shown in Figure 3 and Table 2.

Table 1. Anthropometric and Hemodynamic Characteristics

	Sedentary	Practitioners
Age (yr)	44 ± 12	46 ± 10
Height (cm)	168 ± 10.3	166 ± 7.8
Body mass (kg)	67.1 ± 13.2	62 ± 14.4
BMI (kg/m^2)	23.8 ± 3.1	22.3 ± 3.3
Body Fat (%)	31.5 ± 9.5	25.3 ± 9.1
Systolic BP (mmHg)	118 ± 15	112 ± 12
Diastolic BP (mmHg)	69 ± 12	69 ± 9
Mean BP (mmHg)	84 ± 11	83 ± 10
Brachial PP (mmHg)	50 ± 9	44 ± 10*
Carotid PP (mmHg)	38 ± 8	31 ± 9*
Baseline brachial artery diameter	3.5 ± 1.2	3.8 ± 0.7

Values are means±SD. *$P<0.05$ vs. sedentary.
BMI=body mass index; BP=blood pressure, PP=pulse pressure.

Table 2. Blood Lipids, Glucose, and Glycosylated Hemoglobin

	Sedentary	Practitioners
Total-C (mg/dL)	189 ± 34	190 ± 34
HDL-C (mg/dL)	62 ± 20	67 ± 15
LDL-C (mg/dL)	121 ± 41	120 ± 40
Triglycerides (mg/dL)	89 ± 49	91 ± 28
Glucose (mg/dL)	88 ± 7	91 ± 9
HbA1c (%)	4.5 ± 0.4	4 ± 0.8*

Values are means±SD. *P<0.05 vs. sedentary.
C=cholesterol.

Figure 1. Carotid artery compliance in sedentary adults and yoga practitioners. Carotid artery compliance (CAC) in sedentary adults and yoga practitioners matched for body mass index and age is represented along the Y-axis.

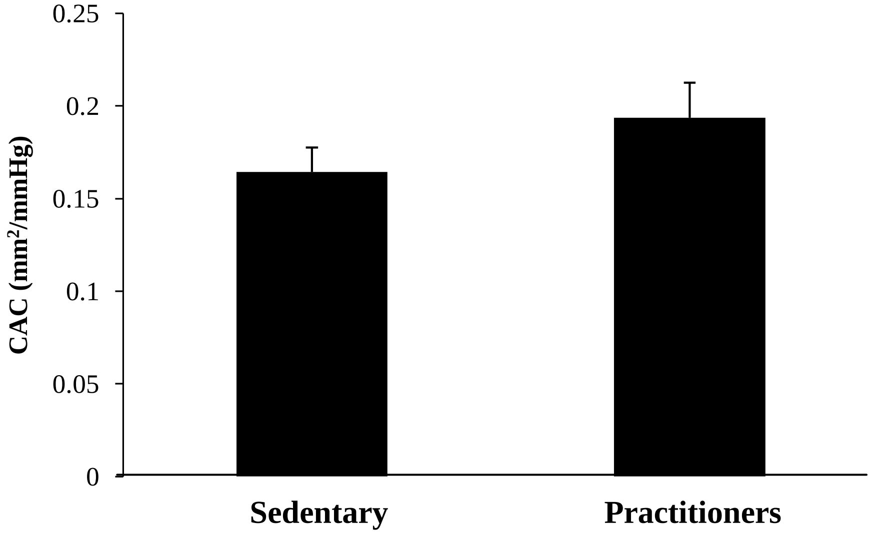


Figure 2. Beta-stiffness in sedentary adults and yoga practitioners. Beta-stiffness is an index of arterial stiffness which eliminates the effect of distending pressure on arterial compliance.

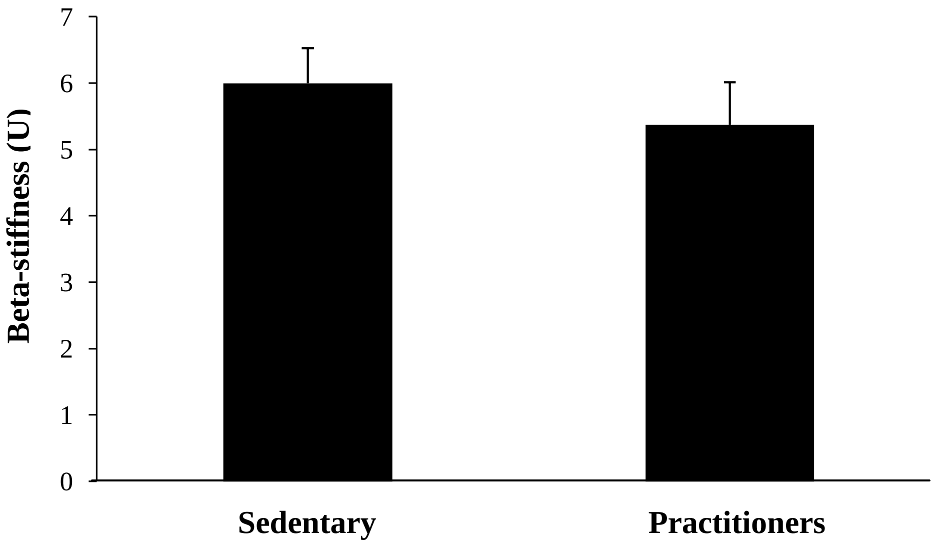
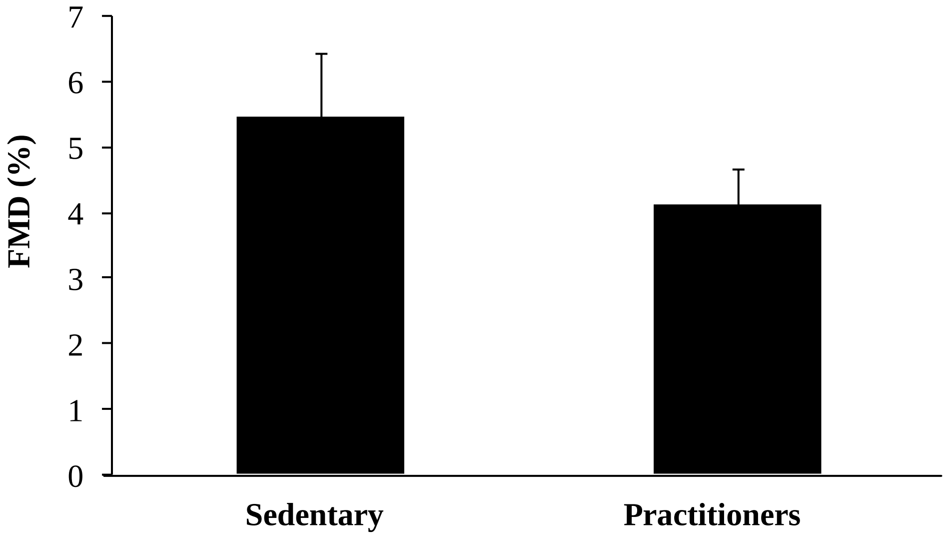


Figure 3. Brachial artery flow-mediated dilation (FMD) in sedentary adults and yoga practitioners. FMD is represented as the percentage of change in brachial artery diameter from baseline following reactive hyperemia.



DISCUSSION

The results from this investigation were not consistent with our original hypotheses. Practitioners of Hatha yoga did not exhibit greater arterial compliance or endothelium-dependent vasodilation. The lack of group differences in arterial compliance does not coincide with previous findings of greater arterial compliance and lower pulse wave velocity among yoga practitioners compared with sedentary controls (41). A potential reason for these discrepant findings is that in the previous study, the groups were not matched for body fatness and other confounding factors. The yoga practitioners had a lower mean BMI than the sedentary group, and the sedentary adults represented an overweight population. Given that overweight and obesity are closely associated with arterial stiffness (32, 124, 140), the differences previously reported could have been accounted for solely by the group differences in body fatness. Therefore, to our knowledge, this is the first investigation to determine the influence of yoga practices on arterial compliance by eliminating this potentially confounding variable.

There was no difference in brachial artery FMD between yoga practitioners and their sedentary peers. To our knowledge, this is the first cross-sectional study to address a role of regular yoga on brachial artery reactivity in healthy adults. Our results suggest that yoga does not appear to modulate endothelium-dependent vasodilatory function. The present study is consistent with the only other study that assessed the effects of yoga on endothelial function. Sivasankaran et al. reported that a 6-week Hatha yoga intervention resulted in a 69%, albeit nonsignificant improvement in endothelium-dependent vasodilation in patients with coronary artery disease (151). Clearly, more studies, especially intervention studies, are needed to fully determine the effects of regular yoga practice on endothelial function.

The lower HbA1c among yoga practitioners is consistent with a role of this activity in regulating glucose homeostasis. Our results are consistent with previous studies that have found that yoga reduced HbA1c and fasting blood glucose levels in adults with metabolic syndrome risk factors and patients with diabetes (52, 87). The lower HbA1c among yoga practitioners may be due to the isometric contractions or the stretching components of the postures as previous studies have demonstrated the effectiveness of isometric training (38) and stretching (18, 75, 80), the main components of most yoga postures, in improving glycemic control. Taken together, these results indicate that yoga may have the potential to be an effective intervention for improving glucose homeostasis.

No group differences in blood pressure were found between yoga practitioners and sedentary controls. These findings are not in agreement with previously published cross-sectional data showing that yoga practitioners had lower systolic and diastolic blood pressures than sedentary controls (41) nor is it consistent with prior intervention studies that have demonstrated that yoga reduces blood pressure in healthy and patient populations (23, 110, 151, 191). In the previous cross-sectional study, the group differences in BMI between the sedentary controls and yoga practitioners could have accounted for the variation in blood pressure between groups. However, in the aforementioned cross-sectional study, the yoga practitioners also had lower blood pressure than the aerobically-trained group to whom their BMI was closely matched. Therefore, despite our discrepant findings, results from most previous studies do indicate that yoga may improve blood pressure.

Limitations

One limitation of this investigation is the cross-sectional nature of the study design. Cross-sectional studies do not fully establish the efficacy of the variable in question and are subject to several potentially confounding factors. We minimized the likelihood of confounding by matching the groups for age and BMI, which could each have affected the measures of vascular health included in this study. Despite the fact that the cross-sectional study design limits our ability to determine the direct effects of the yoga on vascular health, this study does provide a foundation of knowledge upon which future research questions can be generated. Another limitation is the small sample size. After closely matching the groups for age and BMI and excluding the yoga practitioners who engaged in aerobic exercise more than two days per week to minimize potential confounding of these variable on the results, our sample size was reduced. Given that no trends were observed for our main outcome variables of vascular health, it is unlikely that an increase in sample size would have had a substantial impact on our results.

Conclusions

In conclusion, the results from this study indicate that yoga does not modulate vascular health independent of BMI. The lower HbA1c among yoga practitioners merits future study of the potential role of yoga in mediating glucose homeostasis.

Chapter 3: Study 2: 12-week Hatha Yoga Intervention

HYPOTHESES:

1) 12-weeks of Hatha yoga practice will elicit improvements in central arterial compliance in previously sedentary individuals.
2) 12-weeks of Hatha yoga practice will result in augmentations in endothelial function as estimated by brachial artery FMD.
3) These changes will be accompanied by improvements in mental and physical health as estimated by the questionnaires.

SUBJECTS

A total of 28 subjects were studied in the 12-week Hatha yoga intervention. No subjects were taking any cardiovascular medications at the time of the intervention.

Experimental Design

Sedentary subjects were tested before and after a 12-week Hatha yoga intervention. The yoga intervention consisted of 12 weeks of Hatha yoga classes performed at least 3 times per week.

Data and Instrumentation

Subjects were required to fast for at least 12 hours in order to obtain fasting plasma lipids and glucose concentrations. Additionally, fasting was required for the vascular function measures in order to avert the effects of meal content and the hormonal response to food ingestion on vascular function (50, 55, 177). In addition to the previously described measures, subjects participating in the intervention study completed the following 2 questionnaires:

1) The **Pittsburgh Sleep Quality Index** (**PSQI)** is a questionnaire designed to assess sleep quality, which consists of the following components: sleep quality; sleep latency; sleep duration; habitual sleep efficiency; sleep disturbance; use of sleep medication; and daytime dysfunction. Sleep quality is a significant clinical outcome known to affect quality of life. Sleep duration, a component of sleep quality assessed by the PSQI is associated with CVD mortality and all-cause mortality (76). Previous findings have shown that advanced practitioners of yoga defined as having practiced consistently for three years, have better PSQI scores than non-practitioners (171).
2) The **Medical Outcomes Study (MOS) Short-Form (SF-36) Health Survey** is a health and quality of life questionnaire designed to assess medical outcomes from the patients' perspectives (181). It consists of 8 domains: physical functioning (PF); role physical (RP); bodily pain (BP); general health (GH); vitality (VT); social functioning (SF); role emotional (RE); and mental health (MH). The scores from each of these domains were used in the calculation of aggregate scores for mental and physical health (181).

RESULTS

A total of 28 sedentary adults served as participants for this investigation. Of the 28 subjects, 13 completed the 12-week intervention and returned for follow-up testing of which, 2 subjects were male. No subjects were taking any cardiovascular medications at the time of the intervention. Most subjects attended Hatha yoga classes at Yoga Yoga studios here in Austin. Subjects attended an average of two classes per week during the 12-week intervention. One subject has been excluded due to a change in smoking status during the 12-week study period in order to eliminate the effect of this behavior on the vascular parameters studied. Selected subject characteristics are shown in Tables 3 and 4. The mean age of the subjects was 52 years and the BMI was 28.3 kg/m^2.

Results from anthropometric and hemodynamic data are shown in Table 3. There were no changes in BMI, blood pressure, or carotid pulse pressure. Blood lipids and glucose are shown in Table 4. The yoga intervention resulted in a reduction in total cholesterol ($P < 0.05$) and HbA1c ($P < 0.05$). The reduction in triglyceride levels did not attain statistical significance ($P = 0.08$). There were no changes in LDL-cholesterol ($P = 0.14$), HDL-cholesterol ($P = 0.27$), or fasting blood glucose ($P = 0.54$).

Sleep quality and quality of life questionnaire scores are shown in Table 5. There were no changes in sleep quality or in any of the indices of quality of life. However, a trend towards an improvement in mental and physical health was shown although this did not reach statistical significance ($P = 0.10$ and 0.09, respectively).

Carotid artery compliance and brachial artery FMD results are shown in Figures 4 and 5, respectively. There were no alterations in carotid artery compliance ($P = 0.745$), β-stiffness ($P = 0.505$), or brachial artery FMD ($P = 0.441$) as a result of the 12-week yoga intervention.

Table 3. Anthropometric and Hemodynamic Characteristics

	Baseline	12 Weeks
Age (yr)	51 ± 7	
Height (cm)	167 ± 9	
Body mass (kg)	80.1 ± 13.5	79.7 ± 8.4
BMI (kg/m^2)	28.3 ± 5.7	27.8 ± 3.3
Body Fat (%)	42 ± 7	41 ± 8
Systolic BP (mmHg)	122 ± 16	124 ± 14
Diastolic BP (mmHg)	70 ± 11	71 ± 9
Mean BP (mmHg)	87 ± 13	88 ± 11
Brachial PP (mmHg)	53 ± 8	53 ± 7
Carotid PP (mmHg)	41 ± 8	39 ± 6

Values are means±SD.
BMI=body mass index; BP=blood pressure; PP=pulse pressure.

Table 4. Blood lipids, Glucose, and Glycosylated Hemoglobin

	Baseline	12 Weeks
Total-C (mg/dL)	227 ± 37	202 ± 37*
HDL-C (mg/dL)	51 ± 21	37 ± 11
LDL-C (mg/dL)	151 ± 32	136 ± 32
Triglycerides (mg/dL)	163 ± 60	149 ± 77
Glucose (mg/dL)	96 ± 10	97 ± 13
HbA1c (%)	4.5 ± 0.4	4.2 ± 0.4*

Values are means±SD. C=cholesterol; HbA1c=glycosylated hemoglobin A1c.

Table 5. Sleep Quality and Quality of Life Scores

	Baseline	8 Weeks
PSQI score	6 ± 3	5 ± 3
MOS SF-36 scores		
General Health	17 ± 4	20 ± 4*
Mental Health	23 ± 4	25 ± 3*
Physical Function	26 ± 4	28 ± 4*
Vitality	14 ± 4	17 ± 3*
Social Function	8 ± 2	9 ± 2*

Values are means±SD. PSQI=Pittsburgh Sleep Quality Index. MOS SF-36=Medical Outcomes Study Short Form 36-Item questionnaire.

Figure 4. Changes in carotid artery compliance with the 12-week yoga intervention

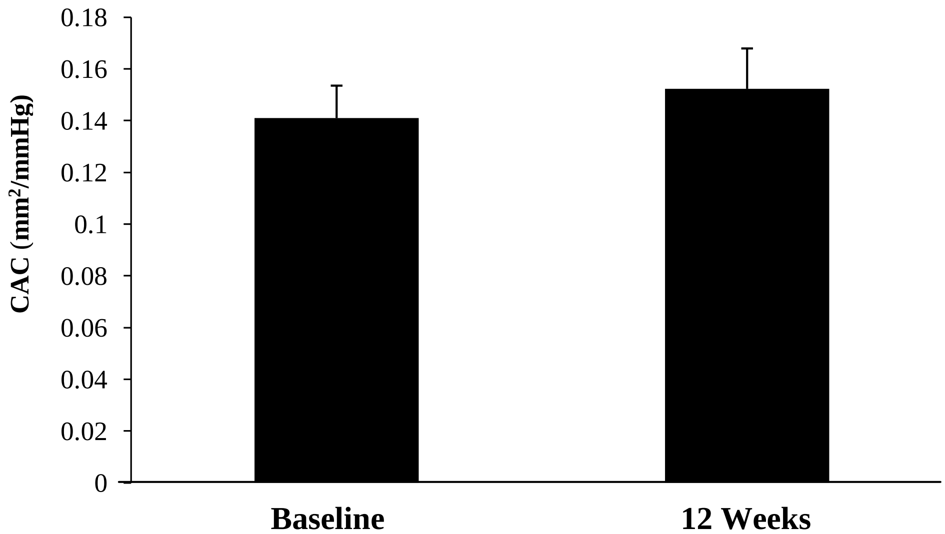
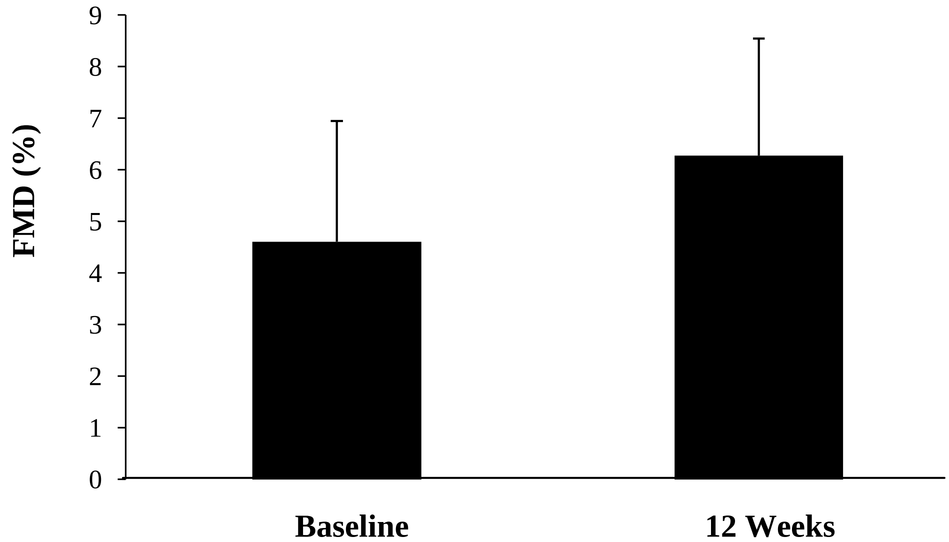


Figure 5. Changes in brachial artery flow-mediated dilation (FMD) after 12 weeks of Hatha yoga



DISCUSSION

Previous cross-sectional data indicated that practitioners of Hatha yoga possessed greater central arterial compliance versus their sedentary peers (41). However, there was no consistent association between Hatha yoga practice and arterial compliance in our cross-sectional study (study #1). Considering that there is no consensus on this issue based on the available cross-sectional studies, an intervention study was needed. To our knowledge, this is the first intervention study to determine the effect of Hatha yoga on arterial compliance. In the present study, arterial compliance did not change with 12 weeks of Hatha yoga. These results are consistent with our previous cross-sectional study. Taken together, Hatha yoga does not appear to affect arterial stiffness in previously sedentary adults.

A lack of change in blood pressure after 12 weeks of Hatha yoga participation is inconsistent with previous findings (13, 23, 64, 110, 151, 191). Using a similar experimental approach, Yang et al. found that 12 weeks of Vinyasa style yoga performed twice per week resulted in reductions in systolic blood pressure in middle-aged adults with at least one cardiometabolic risk factor (191). The subject characteristics from their dataset reveal that the population studied was similar to our sample in terms of age and systolic blood pressure upon study entry. Therefore, given the similarities in subject samples and experimental design, it is inexplicable that our findings did not mimic that of this previous study. However, based on the lack of alteration in arterial compliance, which is an index of the ability of the arteries to buffer cardiac pulsations and regulate blood pressure, it is no surprise that there was no change in blood pressure.

Most yoga intervention studies that have shown reductions in blood pressure have employed populations with pre-hypertension and hypertension (13, 23, 110) and coronary artery disease (151) whereas one previous study has shown reductions in blood pressure in a normotensive population (64). Our sample consisted of sedentary, healthy adults, most of whom were normotensive. This could explain the lack of change in this variable.

Endothelium-dependent vasodilation was unaltered with yoga training, a finding which is consistent with the previous cross-sectional study which showed no difference in this parameter between yoga practitioners and sedentary adults. However, endothelial function tended to increase in patients with coronary artery disease in a previous investigation (151). Given that this is the only previous investigation that has employed this measure, our results may have been better related to this previous study had we used a patient population with presumed endothelial dysfunction.

The design of the intervention utilized in this study precludes our ability to isolate a specific form of Hatha yoga. Most of the subjects were offered a discounted rate at a local yoga studio and attended either beginner Hatha or Vinyasa classes, during which teacher instruction is a major component. A small number of subjects chose to practice at home at least twice per week while following along to a DVD. Given that the subjects did not attend the yoga classes under researcher supervision, the extent to which each yoga posture was performed cannot be determined. Also, the content of the yoga classes are left to the discretion of the yoga instructor and will thus be variable between classes and instructors. For instance, some yoga teachers may include more verbal instruction than others and may thus allocate less class for postures than others. We acknowledge that this aspect of our intervention introduces a certain element of variability and may limit our ability to compare our results to those from previous studies. However, we deemed it a more generalizable approach as most beginners are placed in yoga studio and learn yoga postures from a number of different instructors. Even though previous studies have employed various forms of Hatha yoga from simple breathing exercises (pranayama) to more intense Vinyasa classes and to date, none have studied the effects of any of these forms of yoga on vascular health in healthy adults.

Limitations

The dropout rate for the intervention was substantial at over 50%. Most subjects reported a lack of time as the reason for their discontinuance of the yoga classes. No subjects were compensated for their participation in this study. Moreover, they were responsible for the costs of the yoga classes. Perhaps if we had provided the classes for the subjects under direct researcher supervision along with compensation, the dropout rate would have been lower and our sample size would have been larger.

Another limitation of this study is the lack of control group. This study was intended to serve as a pilot study for future interventions as this research question had not yet been addressed. If the results from the current investigation showed changes in vascular health as a result of the yoga intervention, the addition of a control group would have increased the validity of those findings. However, due to the lack of change in our key outcome variables, it is unlikely that the addition of a control group would have been beneficial in this instance.

Conclusions

In conclusion, based on the results from the current investigation in conjunction with the findings from our cross-sectional study that Hatha yoga does not appear to alter arterial stiffness or vasoreactivity as assessed by carotid artery compliance and brachial artery FMD in healthy adults. However, it may improve subjective measures of mental and physical health and sleep quality, which may lead to improvements in the quality of life.

Chapter 4: Study 3: 12-week Bikram yoga intervention

Introduction

Obesity is rapidly spreading in the U.S. and currently affects over one third of the population (45). Obesity contributes to the atherosclerotic process through its effects on vascular endothelial function (95, 157) and arterial stiffness (125, 140). Linking obesity and CVD are its associated characteristics of chronic, low-grade inflammation (67), insulin resistance (100, 158), and elevations in adrenergic stimulation (100, 148). Given the magnitude of this healthcare concern in the U.S., interventions aimed at reducing the risks associated with it are of vital importance.

Bikram yoga is a form of Hatha yoga in which a series of 26 postures are performed in a heated sauna-like environment. As previous studies have shown reductions in blood pressure (13, 23, 110, 151, 191) and inflammation (88, 132, 133), and improvements in glycemic control (87) with Hatha yoga, few studies have attempted to unveil the additional health benefits of Bikram yoga. A previous investigation showed improvements in leg strength and standing balance time after an 8-week Bikram yoga intervention (65). Although there is a paucity of empirical data suggestive of the efficacy of this form of yoga in improving physical and mental health, the added component of the heat may serve as stimulus for additional physiological adaptations above other nonheated forms yoga.

Sauna therapy has been shown to enhance endothelial function in men with coronary risk factors (78) and in patients with chronic heart failure (90) while warm water immersion has been shown to attenuate high-fat diet induced glucose intolerance in an animal model through increases in heat shock protein (58) and reduce HbA1c levels in a diabetic patient population

(73). These results suggest that the thermal component of Bikram yoga may attenuate the endothelial dysfunction and glucose intolerance in obese subjects and thereby reduce the risk associated with this disease. Therefore, the purpose of this study is to determine whether Bikram yoga will elicit improvements in vascular endothelial function and glucose tolerance in obese adults.

HYPOTHESES:

1) Bikram yoga will improve brachial artery endothelium-dependent dilation in obese individuals.
2) Central arterial compliance and arterial stiffness will be improved in the obese group as a result of 8 weeks of consistent practice of Bikram yoga.
3) 8 weeks of Bikram yoga will improve glucose tolerance and HOMA-IR in the obese group.

SUBJECTS

Sixty currently sedentary men and women between the ages of 20 and 70 years were recruited from the Austin area for this intervention study. Half (n=30) of the subjects were lean and apparently healthy defined as having a BMI in the range of 18.5 to 24.9 kg/m^2 with no apparent CVD risk factors, and the other half (n=30) will be classified as obese defined as having a body mass index equivalent to or above 30 kg/m^2 or a waist circumference equivalent to or above 88 cm or 100 cm for women and men, respectively.

Experimental Design

Both groups underwent an 8-week Bikram yoga intervention in which they must attend a minimum of three classes per week after baseline testing with the lean group serving as the healthy controls. All yoga classes were completed at Pure Bikram Yoga or Yoga Groove studios in the Austin area based on the personal preference of the subjects. Both yoga studios had agreed to provide a discounted rate of $99 for 10 weeks of unlimited classes to all study participants. At the end of the intervention, both groups completed follow-up testing. In addition to the other measures, a sub-sample of participants was tested for maximal oxygen consumption before and after the 8-week intervention.

Data and Instrumentation Subjects were required to complete two testing sessions, and a 3-day diet record was completed three days prior to the second session, which consisted of vascular function testing. Subjects were required to fast for 12-hours prior to the first two sessions (oral glucose tolerance test and vascular measures). In addition to the aforementioned testing measures, subjects for this intervention study completed the following:

1) **Research Health Questionnaires** were completed by each subject prior to their participation in this investigation. Exclusion from this study was conditional upon the following: i) pregnancy; ii) uncontrolled hypertension (blood pressure >160/100 mmHg while on hypertensive medications); iii) infection within the previous 4 weeks; iv) having adrenal or endocrine tumors; v) renal disease; vi) prior myocardial infarction (heart attack); vii) known coronary artery disease; viii) chronic heart failure; ix) personal history of stroke; x) personal history of cardiac arrhythmias; xi) uncontrolled diabetes (chronic hyperglycemia while on diabetic medications); xii) diabetic neuropathy; xiii) personal history of psychosis; xiii) orthopedic limitations that prevent them from being able to perform the yoga postures; and xiv) heat intolerance.
2) **Blood samples** were taken via venapuncture using 20 and 22 Gauge Saf-T-Intima Closed IV Catheter Systems with Y Adapters (Becton Dickinson Infusion Therapy Systems,

Sandy, Utah). After catheter insertion, pure saline was infused using a pre-filled, 3mL 0.9% saline syringe (Becton, Dickinson and Co., Franklin Lakes, NJ) in order to flush the tube and prevent clot formation. Blood cholesterol, triglyceride, and glucose levels and HbA1c were analyzed using the methods described above. In addition, fasting plasma insulin concentrations were determined using insulin antibody coated tube 125I RIA kits (MP Biomedicals, LLC, Solon, OH). Insulin resistance was estimated using the homeostasis model assessment-insulin resistance (HOMA-IR) (109) in the following equation: (Fasting plasma insulin*Fasting plasma glucose)/22.5

3) **A 2-hour oral glucose tolerance test (OGTT)** was administered to each subject to obtain an index of glucose tolerance. After the initial blood sample was taken and analyzed, the subject ingested a 75-g glucose solution (Azer Scientific Inc., Morgantown, PA) and blood samples (1 EDTA tube) was taken every 30 minutes and analyzed for plasma glucose concentrations.

4) **Arterial stiffness** was determined via pulse wave velocity (PWV) using the VP-2000 (Colin Medical Instruments, San Antonio, TX). Pressure waveforms obtained from blood pressure sensors placed over the carotid and femoral arteries were analyzed. The distance between the two sites (carotid and femoral arteries) was measured and taken into account in the calculation of carotid-femoral PWV. In addition, blood pressure cuffs were placed around the upper arms and ankles and used to determine brachial-ankle PWV. Both carotid-femoral and brachial-ankle PWV are indices of central arterial stiffness while the latter is indicative of peripheral arterial stiffness.

5) **Low-back and hamstring flexibility** was tested using a sit-and-reach protocol (2) after the subject warmed up with a 5-minute brisk walk on a treadmill located in our

laboratory. Subjects will sit on the floor with their head and torso pressed against a wall. Their legs were extended straight out in front of them, and their feet were placed on the sit-and-reach testing device 10 to 12 inches apart. The subjects then extended both arms out in front of them and reach forward as far as possible and held for two seconds. The best of two trials was recorded.

Statistical Analyses

ANOVA was utilized to determine group differences in baseline characteristics and ANOVA with repeated measures was used to determine differences between baseline and post-intervention means.

RESULTS

A total of 70 subjects were recruited for the current study of which 36 were lean and 34 were obese adults between the ages of 18 and 60 years. Of the 70 subjects, 52 (25 obese, 27 lean) completed the 8-week intervention and returned for follow-up testing. Males accounted for 16% and 22% of the obese and lean subjects, respectively. Of the 25 obese subjects, 4 were taking blood pressure medications, and 5 were taking cholesterol-lowering medications. All medications were continued throughout the 8-week intervention period. Two of the obese subjects discontinued their blood pressure medications during the intervention and their blood pressure data have been excluded from the group means. One of subjects in the lean group began hormone replacement therapy during the 8-week intervention and has been excluded from the results. Baseline selected subject characteristics are shown in Table 6.

Body fat percentage, systolic and mean arterial blood pressures, total cholesterol, triglycerides, and blood glucose levels were all higher in obese subjects compared to the lean group ($P<0.05$). Intervention results for blood pressures and anthropometric characteristics are shown in Table 7. There were no changes in body composition or blood pressure in either the lean or obese groups after the 8-week yoga intervention.

Blood lipids and glucose and plasma insulin concentrations are shown in Table 8. There were no changes in blood lipid profiles in the obese group. Total- and LDL-cholesterol were reduced in the lean subjects ($P<0.05$). Fasting insulin levels remained unchanged as a result of the intervention in both groups. HOMA-IR decreased in the lean subjects, although not significant ($P = 0.06$), but not in the obese group. Flexibility is also shown in Table 8 and improved in both lean and obese subjects ($P<0.05$).

Arterial stiffness indices are shown in Table 9 and include carotid-femoral and brachial-ankle pulse wave velocity and β-stiffness. Arterial stiffness was unaltered by the 8-week intervention in both lean and obese subjects. Carotid artery compliance as shown in Figures 6 and 7 also remained the same in both lean ($P = 0.17$) and obese subjects ($P = 0.51$) after the 8-week yoga intervention.

Sleep quality and quality of life questionnaire scores for all lean and obese subjects are shown in Table 10. Sleep quality did not change as a result of the Bikram yoga intervention. However, general health, mental health, physical function, vitality, and social function all increased as a result of the 8-week intervention ($P<0.05$).

Brachial artery FMD results are shown in Figures 8 and 9. Brachial artery FMD tended to increase in the obese subjects. However, this observed trend did not attain statistical significance ($P = 0.10$). Brachial artery FMD was unaffected by the 8-week yoga intervention in the lean subjects ($P = 0.919$).

Glucose tolerance results are shown in Figures 10 and 11. There were no changes in glucose tolerance in the lean or obese groups as a result of the yoga intervention at all time points. However, an improvement was shown at 60 minutes in obese subjects that did not reach statistical significance ($P = 0.056$).

Table 6. Selected subject characteristics

	Lean	Obese
Age (yr)	34 ± 12	42 ± 12*
Height (cm)	167 ± 9	167 ± 8
Body mass (kg)	62.8 ± 10.6	93.3 ± 16.5*
BMI (kg/m^2)	22 ± 2.1	33.5 ± 4.3*
Body Fat (%)	29.3 ± 8	44.7 ± 6.2*
Systolic BP (mmHg)	109 ± 9	120 ± 18*
Diastolic BP (mmHg)	64 ± 8	70 ± 12
Pulse Pressure (mmHg)	45 ± 6	51 ± 9
MAP (mmHg)	79 ± 8	86 ± 13*
Total-C (mg/dL)	181 ± 35	205 ± 45*
HDL-C (mg/dL)	63 ± 19	54 ± 19
LDL-C (mg/dL)	118 ± 31	136 ± 42
Triglycerides (mg/dL)	80 ± 23	117 ± 72*
Glucose (mg/dL)	86 ± 8	101 ± 36*
Insulin (µIU/mL)	18.2 ± 4.3	31.4 ± 18.6

Values are means±SD. BMI=body mass index, BP=blood pressure, MAP=mean arterial pressure, C=cholesterol.
*P<0.05 vs.lean subjects.

Table 7. Changes in selected subject characteristics with the Bikram yoga intervention

	Baseline	8 weeks	Baseline	8 weeks
Body mass (kg)	62.8 ± 10.6	63.3 ± 11	93.3 ± 16.5	93.7 ± 16.6
BMI (kg/m^2)	22 ± 2.1	22.6 ± 2.3	33.5 ± 4.3	33.1 ± 4.6
Body Fat (%)	29.3 ± 8	29 ± 8.5	44.7 ± 6.2	44.1 ± 6.7
Systolic BP (mmHg)	109 ± 9	109 ± 9	120 ± 18	118 ± 14
Diastolic BP (mmHg)	64 ± 8	64 ± 8	70 ± 12	67 ± 10
MAP (mmHg)	79 ± 8	79 ± 8	86 ± 13	84 ± 10
Pulse Pressure (mmHg)	45 ± 6	45 ± 4	51 ± 9	50 ± 10

Values are means±SD. BMI=body mass index, BP=blood pressure, MAP=mean arterial pressure.

Table 8. Changes in blood lipids, glycemic control, and flexibility in lean and obese subjects with the Bikram yoga intervention

	Lean		Obese	
	Baseline	**8 weeks**	**Baseline**	**8 weeks**
Total-C (mg/dL)	181 ± 35	167 ± 24*	205 ± 45	197 ± 35
HDL-C (mg/dL)	63 ± 19	61 ± 22	54 ± 19	50 ± 17
LDL-L (mg/dL)	118 ± 31	90 ± 31*	136 ± 42	127 ± 35
Triglycerides (mg/dL)	80 ± 23	84 ± 26	117 ± 72	127 ± 62
Glucose (mg/dL)	86 ± 8	83 ± 6	101 ± 36	97 ± 28
HbA1c (%)	4.5 ± 0.5	4.7 ± 0.5	5 ± 0.8	5.1 ± 1.2
Insulin (µIU/mL)	18.2 ± 4.3	16.4 ± 4.8	31.4 ± 18.6	24.5 ± 12.3
HOMA-IR	3.9 ± 1.1	3.3 ± 1.0	7.7 ± 5.9	6.2 ± 2.8
Sit-and-Reach (cm)	33 ± 11	43 ± 12*	25 ± 11	31 ± 10*

Values are means±SD. C=cholesterol, HbA1c=glycosylated hemoglobin, HOMA-IR=homeostatic model of the assessment of insulin resistance.

Table 9. Changes in arterial stiffness with the Bikram yoga intervention

	Lean		Obese	
	Baseline	**8 weeks**	**Baseline**	**8 weeks**
Carotid-Femoral PWV (cm/s)	833 ± 117	838 ± 126	900 ± 212	986 ± 304
Brachial-Ankle PWV (cm/s)	1135 ± 121	1135 ± 136	1182 ± 186	1165 ± 188
β-stiffness (U)	4.5 ± 0.8	□ 4.3 ± 1	5.7 ± 0.3	5.6 ± 2.0

Values are means±SD. PWV=pulse wave velocity.

Table 10. Changes in sleep quality and quality of life with the Bikram yoga intervention

	Baseline	8 Weeks
PSQI scores		
Sleep Quality	7 ± 4	7 ± 4
MOS SF-36 scores		
General Health	19 ± 4	20 ± 2*
Mental Health	24 ± 4	25 ± 3*
Physical Function	25 ± 2	26 ± 1*
Vitality	16 ± 2	17 ± 3*
Social Function	9 ± 2	10 ± 2*

Values are means±SD. PSQI=Pittsburgh Sleep Quality Index,
MOS SF-36=Medical Outcomes Study Short Form 36-Item Questionnaire.

Figure 6. Changes in carotid artery compliance (CAC) in lean subjects with Bikram yoga

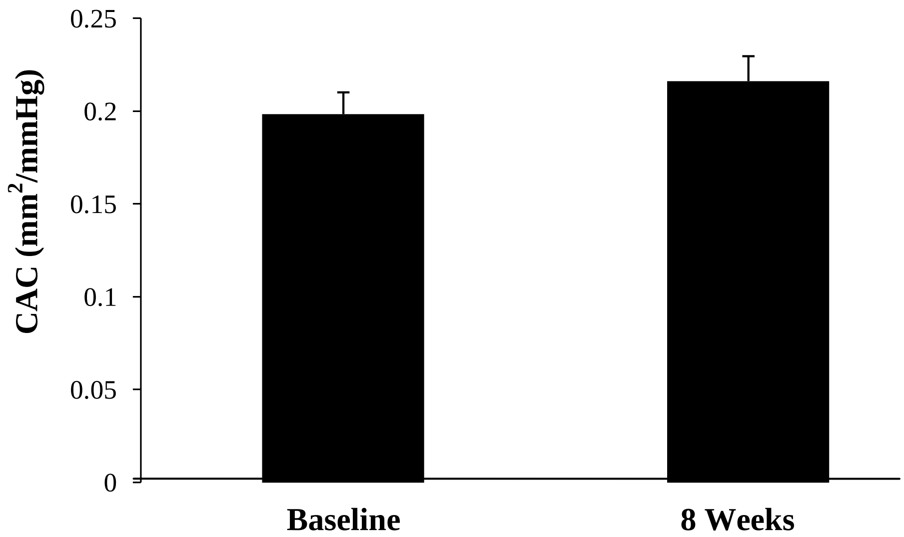


Figure 7. Changes in carotid artery compliance in obese subjects with the Bikram yoga intervention

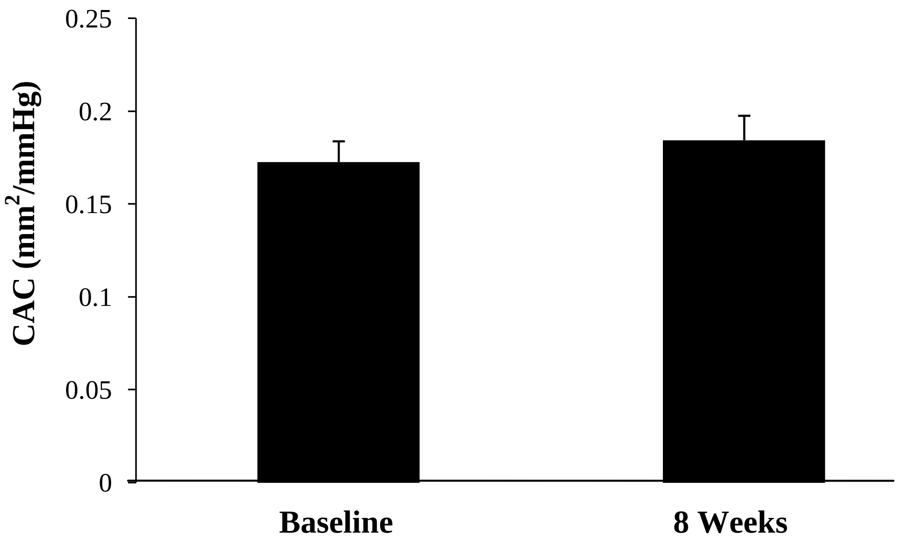


Figure 8. Changes in brachial artery FMD in lean subjects with the Bikram yoga intervention

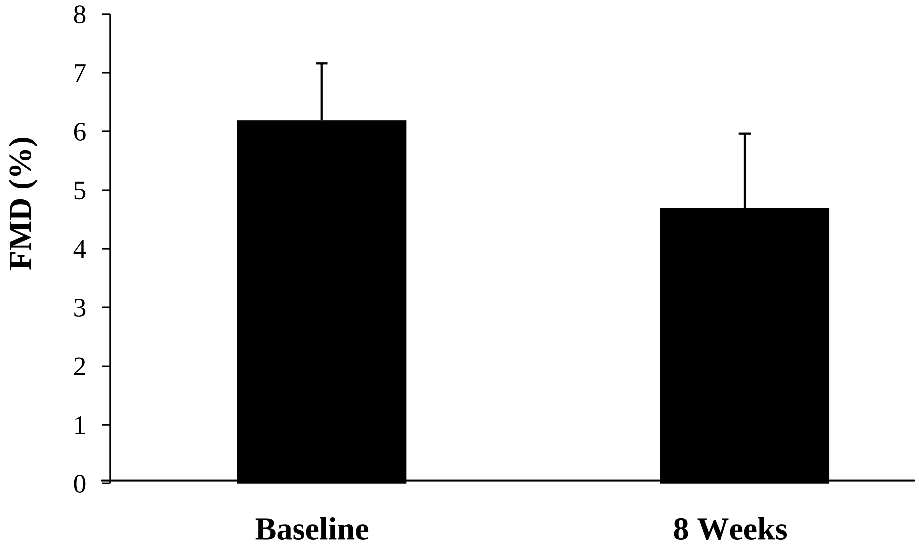


Figure 9. Changes in brachial artery FMD in obese subjects with the Bikram yoga intervention

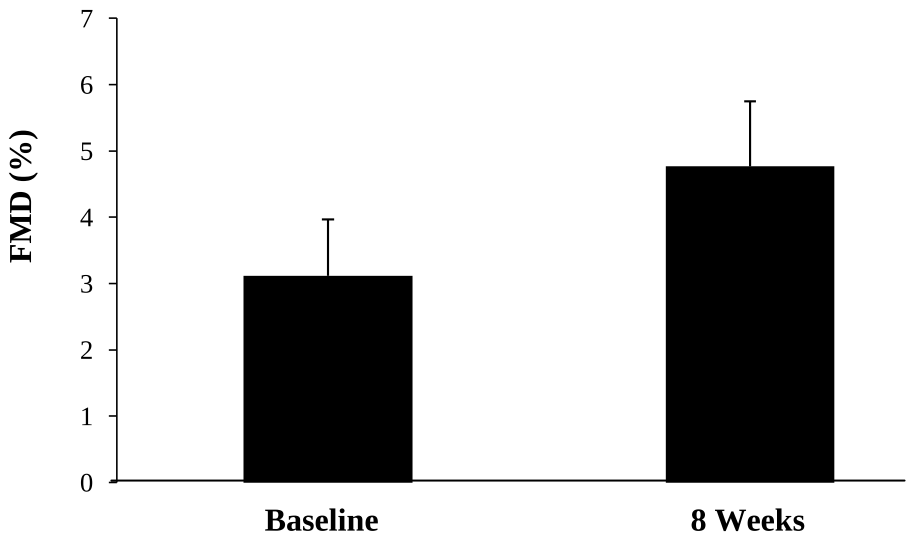


Figure 10. Changes in glucose tolerance in lean subjects with the Bikram yoga intervention

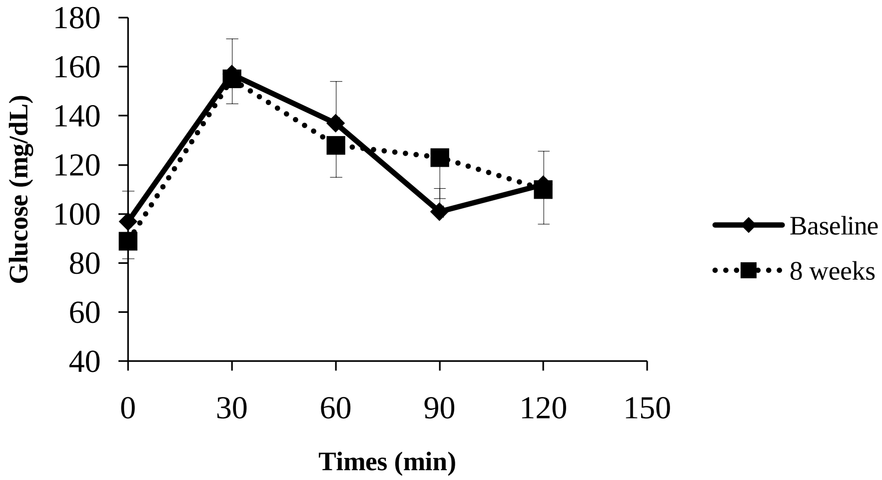
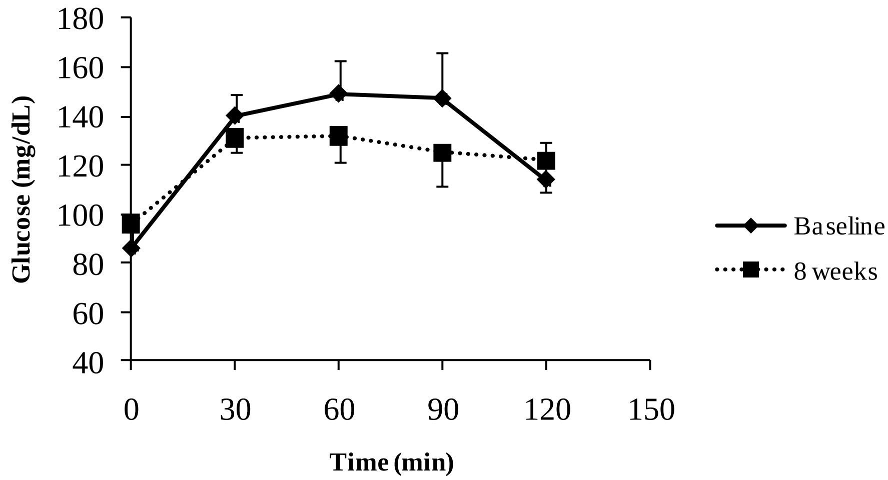


Figure 11. Changes in glucose tolerance in obese subjects with the Bikram yoga intervention



DISCUSSION

There were no changes in arterial stiffness as a result of the Bikram yoga intervention. This finding does not concur with previously published cross-sectional data which showed that practitioners of yoga had lower arterial stiffness and greater arterial compliance than sedentary individuals (41). As previously stated, the results of that cross-sectional study reveal that the two groups were not well matched for BMI and that their finding of lower arterial stiffness among yoga practitioners could have been accounted for in part or in total by the group differences in this variable.

We sought to unveil the effectiveness of yoga in reducing arterial stiffness based on previously published data indicating that 12 weeks of stretching resulted in augmentations in carotid artery compliance through reductions in carotid pulse pressure (29). Stretching is a major component of most yoga postures employed in yoga. Another investigation also showed a positive correlation between flexibility and arterial stiffness (190). Taken together, these findings are indicative of a link between skeletal muscle flexibility and the distensibility of the central arteries. We have since conducted 3 studies examining this possible relationship and have consistently found that yoga, a mode of exercise consisting mostly of static stretching, does not mediate arterial stiffness in healthy or obese adults.

Our findings suggest that one or many additional factors could be driving the previously reported correlation between flexibility and arterial stiffness. It could simply be explained higher levels of physical activity among the older adults in that group which could be associated with an increased joint range of motion and that these physical activity levels could be driving the association between arterial stiffness and flexibility.

Pulse wave velocity was included in this final intervention study due to its recognition in research literature as being the “gold standard” measurement modality for arterial stiffness. Although it has been referred to as the “gold standard”, it still remains an indirect measure of arterial stiffness and one might argue that carotid artery compliance via ultrasonography is a more direct measure of the stiffness of the artery as it takes into account the changes in the arterial diameter over the course of each cardiac cycle along with the change in pressure. Arterial compliance better reflects the elastic properties of the vessel and the ability of the artery to buffer pulsations initiated from the left ventricle. Our results show that Bikram yoga did not elicit changes in any of the arterial stiffness measures in lean or obese adults.

The mechanisms contributing to arterial stiffness include adrenergic stimulation of alpha receptors along the vessel wall resulting in increased vascular tone (9, 53, 108), endothelin-1 (106, 112), nitric oxide (93, 94, 186), angiotensin-II (99, 166) and vessel wall composition, i.e. elastin and collagen content. Of these factors, sympathetic innervation, endothelin-1, and nitric oxide bioavailability are subject to change with aerobic exercise. Given that yoga does not affect arterial stiffness, yoga, unlike aerobic exercise, does not seem to mediate the factors contributing to arterial stiffness or it may not be a sufficient stimulus for significant alterations in these variables.

Endothelium-dependent vasodilation as indicated by brachial artery FMD tended to increase in the obese subjects but not in the lean individuals. This increase in FMD, however, did not reach statistical significance due in part to the inherent variability of this measure. This finding is indicative of a role of yoga in mediating vasoreactivity. Of the factors influencing FMD, NO is of key importance due its vasoprotective capacity. Although an indirect measure, FMD provides an estimate of endogenous NO production and bioavailability. Obesity is associated with endothelial dysfunction potentially due to chronic low-grade inflammation, which leads to ROS production and NO scavenging. This low-grade inflammation also increases the activation of stress kinases, which facilitate the development of insulin resistance.

Previous studies have shown that yoga reduces inflammation in chronic heart failure patients (132) and attenuates the inflammatory response to mental stress in healthy adults (88). This could provide a mechanistic link between yoga and FMD. However, in our previous study, which employed a 12-week Hatha yoga intervention, there were no improvements in this measure. The two interventions were similar in that both included 24 Hatha yoga sessions, but the addition to this study was the thermal component as Bikram yoga is practiced in a heated environment.

Previous studies have shown that aerobic exercise improves FMD. A mechanism for this is that the sustained increases in cardiac output during bouts of aerobic exercise result in upregulations of eNOS due to the increases in shear stress along the vessel wall. Aerobic exercise is not the only stimulus for sustained increases in blood flow. A previous study utilized warm water immersion as the stimulus for increases in blood flow in the forearm (54). In order to demonstrate the role of shear stress in FMD adaptations, they submerged both arms in warm water while occluding one arm to prevent the increase in blood flow during immersion. They found that endothelial function only improved in the unoccluded arm which confirms that hypothesis that shear stress is a major component of FMD augmentations.

Yoga is very different from aerobic exercise in that it performed intermittently. Although the isometric contractions involved in the postures elicit increases in cardiac output, they are not sustained over the entire session as there is typically a break in between postures that involves standing in place or lying in the supine position. Perhaps, a more continuous form of yoga like

Vinyasa flow in which there is constant movement during each class would serve as a better stimulus for shear stress induced alterations in endothelial function.

Sauna therapy in the absence of exercise improves FMD in individuals with coronary risk factors and in patients with chronic heart failure (77) due in part to an upregulation of eNOS (89). Based on the results from both of the current yoga intervention studies, we surmise that in addition to the finding that yoga does not alter endothelial function, the thermal component of Bikram yoga is not enough of a stimulus to induce improvements in vascular function either. The nature of sauna therapy employed in previous studies is different from the heat experienced during a Bikram yoga class. Previous studies that have shown improvements in FMD have utilized dry saunas set to temperatures of approximately 61 degrees Celcius, which is hotter than the typical temperature of a yoga class, which is around 40 degrees Celcius.

Despite the temperature difference between the two interventions, we proposed that similar adaptations would occur given that although the temperature is a bit cooler than previous studies, the subjects are exercising in this environment, which would generate more heat and cause similar adaptations to occur. However, such was not the case.

A previous isometric handgrip training study employed an 8-week intervention in which handgrip exercises were performed at a rate of 30 grips per minute for 30 minutes 3 days per week while occluding one arm to prevent increases in blood flow as a result of the handgrip exercises(167). They found that FMD increased in the uncuffed arm after two weeks of training, remained elevated up to week 6, and returned to baseline levels by week 8. These findings lend support to the notion that exercise-induces augmentations in FMD are mediated by increases in shear stress as no changes were seen in this parameter in the uncuffed arm. They also showed that, although FMD returned toward baseline values, the dilatory capacity of the brachial artery as measured during handgrip exercise while the arm is occluded, continued to increase. The authors suggested that the initial changes in FMD result from functional changes such as rapid increases eNOS activity and NO availability while the subsequent adaptation of the return toward baseline was the result of structural adaptations in the vessel that reduce the magnitude of the shear stress stimulus. The exercise mode employed in this intervention suggests that isometric training has the capacity to augment endothelial function, at least in short term, but lacks the ability to capture a long-term adaptation in this measure.

Shear rate is a calculated variable taking into account the blood flow velocity during reactive hyperemia following cuff deflation and is inversely proportional to the baseline diameter of the artery. Since their results showed no changes in baseline diameter or shear rate, it does not appear that structural changes within the vessel accounted for the changes in FMD in the later stages of the intervention. However, their results lend insight into the pattern of changes in FMD that may not be captured by simply performing pre- and post-intervention measurements. Perhaps if we had included repeated measurements at 2-week intervals, we would have discovered the same pattern that FMD increased initially, but then returned toward baseline levels. We decided not to pursue this due to the lack of clinical significance of this finding. If the FMD response, which is indicative of NO availability and CVD risk returns to baseline by week 8 due to proposed structural changes that have yet to be unveiled and exert no effect on shear rate, the applicability of this finding to at risk populations for future research would be lacking.

Previous results indicative of the effect of isometric training on FMD have been inconsistent. Increases in FMD have been shown in hypertensive adults (117) while no changes have been seen in healthy, normotensive individuals (114, 116). If we had limited this intervention to hypertensive adults, we might have seen similar results of augmentations in endothelial function similar to these previous investigations given the magnitude of proportion of isometric muscle contractions involved in yoga postures.

The notion of endothelial adaptations to isometric exercise training was pursued in earlier studies due to preceding results of the efficacy of this exercise mode in reducing blood pressure. Endothelial function was investigated as the possible mechanism underlying these blood pressure reductions in previous studies. Consistent with the lack of change in endothelial function in the present study, changes in blood pressure were also not observed. Few of the obese subjects were taking blood pressure medications, which they continued throughout the 8-week intervention. However, upon the exclusion of these few medicated subjects, the results remained consistent and no changes were observed in blood pressure as a result of the intervention. In addition, isometric training has been shown to reduce blood pressure (115) and improve endothelial function in medicated hypertensive patients (117). Therefore, we decided not to exclude individuals on blood pressure lowering medications from this study.

Another potential reason for the lack of change in endothelial function in both of the current yoga intervention studies is the previous finding that the change in FMD with isometric handgrip training was limited to the arm which performed the handgrip exercises studies showing improvements in FMD with isometric handgrip training have been limited to the arm involved in the handgrip exercises while no improvements in FMD were shown in the untrained arm (116). Most yoga postures involve isometric contractions of leg muscles, while only few of the postures include isometric contractions of the arm muscles. Therefore, based on the results from this investigation, we speculate that if yoga does elicit increases in FMD, that these alterations, like previous studies, could be limited to the lower limbs. We might have observed changes had we measured the FMD response in the popliteal or femoral arteries.

Glucose tolerance remained unchanged in the obese subjects as a result of the yoga intervention. Previous studies have shown improvements in glycemic control in diabetic patients and in glucose tolerance in high-fat fed animals. In addition, studies have shown that isometric exercise training (38), which a large component of yoga postures, improves glucose tolerance. Based on these findings, we hypothesized that as a combination of the two, that Bikram yoga would improve glucose tolerance in obese subjects who are likely glucose intolerant.

Glucose tolerance and HOMA-IR, which is indicative of fasting glucose and insulin levels, remained unchanged by the Bikram yoga intervention in both groups. To our knowledge, this study was the first attempt to determine the effectiveness of yoga in improving glucose tolerance in obese individuals. We hypothesized that glucose tolerance, which is indicative of insulin action, would improve as a result of the thermal component of Bikram yoga based on results from a previous study showing improvements in glucose tolerance in high-fat fed animals through increases in heat shock protein mediated inhibition of stress kinases which impair insulin signaling (58). In addition, isometric training and stretching have both been shown to ameliorate glycemic control (18, 38, 75, 80). Our results collectively show that neither the yoga postures nor the thermal therapy component of Bikram yoga was effective in improving glucose tolerance in obese adults.

There was also no change in body composition in either group as a result of the 8-week intervention. This could account for the lack of change in glucose tolerance as muscle tissue accounts for the majority of glucose uptake. We suspect that an increase in lean body mass would have potentially led to improvements in glucose tolerance, and since this did not occur, it is no surprise that glucose tolerance remained the same.

Despite the lack of change in body composition, flexibility improved in both groups. Based on the previous finding that passive stretching of skeletal muscle increases induces GLUT4 translocation and stimulates muscle glucose uptake via Akt activation independent of PI3-K (18, 75, 80), we expected these increases in flexibility to be accompanied by increases in skeletal muscle glucose uptake. However, the results from the glucose tolerance tests did not demonstrate this.

Most of the subjects in this intervention study were new to Bikram yoga and for this reason, time had to be allotted for the subjects to acclimate to the heat and learn the postures. Therefore, we speculate that a longer intervention would have been more informative of the effects of Bikram yoga on all of the outcome variables since this would have given the subjects more time to become familiar with the postures and become accustomed to the heat. For this reason, more research is necessary which allows a longer duration for the intervention for subjects who are unfamiliar with the practice.

Limitations

We do acknowledge that the current study has its limitations. Firstly, diet was not controlled during the intervention. All subjects were instructed not to alter their diets in any way during the 8-week period and 3-day food logs were given before and after to gain insight into this potentially confounding factor. However, a more controlled approach would have been to provide the subjects with meals over the course of the 8 weeks to ensure their diets were unaltered. Based on the results from lipid profile and endothelial function, it does not appear that the subjects in this investigation supplemented their exercise with diet improvements, but since we did not determine food intake over the entire 8 weeks, we are unable to determine this with certainty. Another limitation is that the lack of a control group. No control group was included in this investigation so we were unable to determine the variability of the measurements over time. Given that no significant changes occurred in any of the vascular measures, a control group would have added little to the validity of the findings.

Conclusions

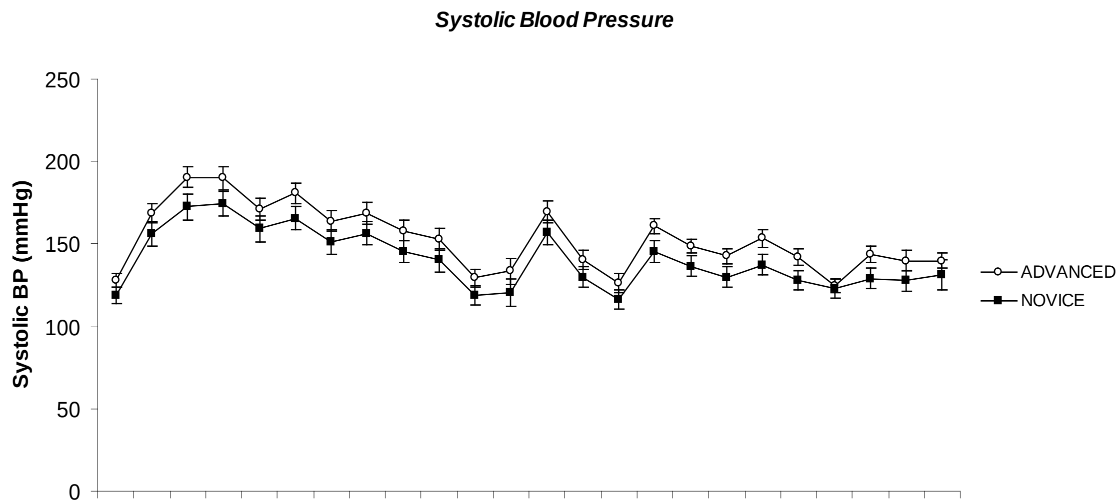
1. Hatha yoga does not modulate arterial stiffness as indicated by pulse wave velocity, arterial compliance, or β-stiffness. Perhaps studies of longer durations may demonstrate a change in these variables, but 8 and 12 weeks are not of sufficient duration to elicit improvements in these variables in lean or obese adults.
2. Hatha yoga also does not augment brachial artery FMD in healthy or in lean adults as indicated by the results from the cross-sectional and intervention studies.
3. Bikram yoga may, however improve endothelial function due to the added component of the heat, but larger scaled studies are needed in to make this determination.

Appendix A

Warrior III

http://www.thebonearchitect.wordpress.com

Appendix B


Systolic Blood Pressure
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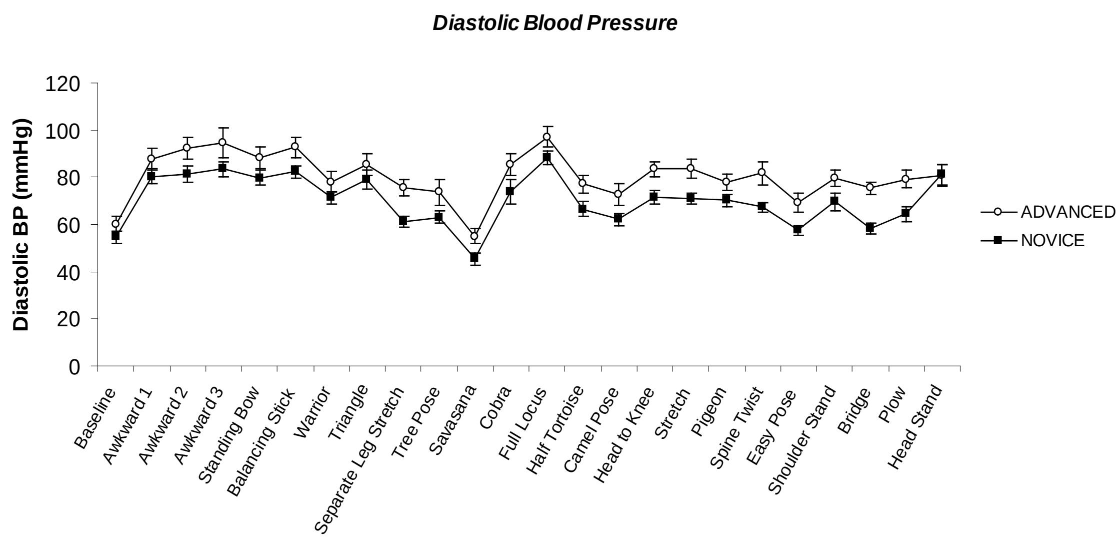
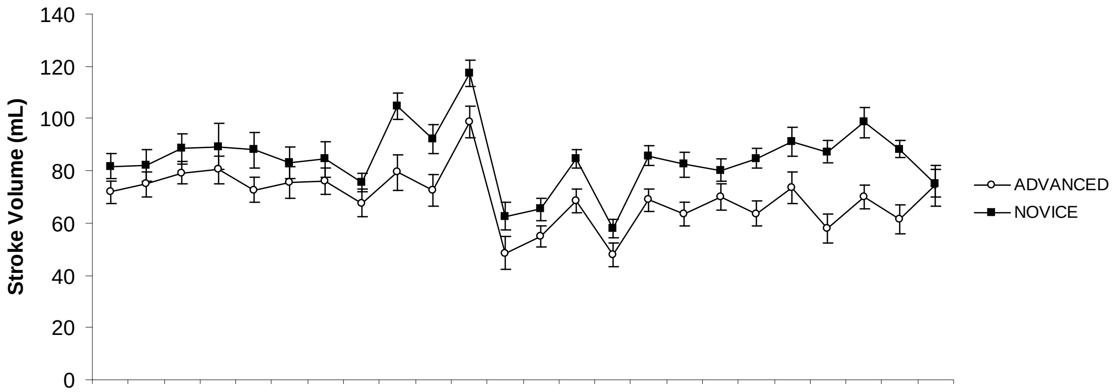
200
150
100
50
0
Systolic BP (mmHg)
ADVANCED
NOVICE

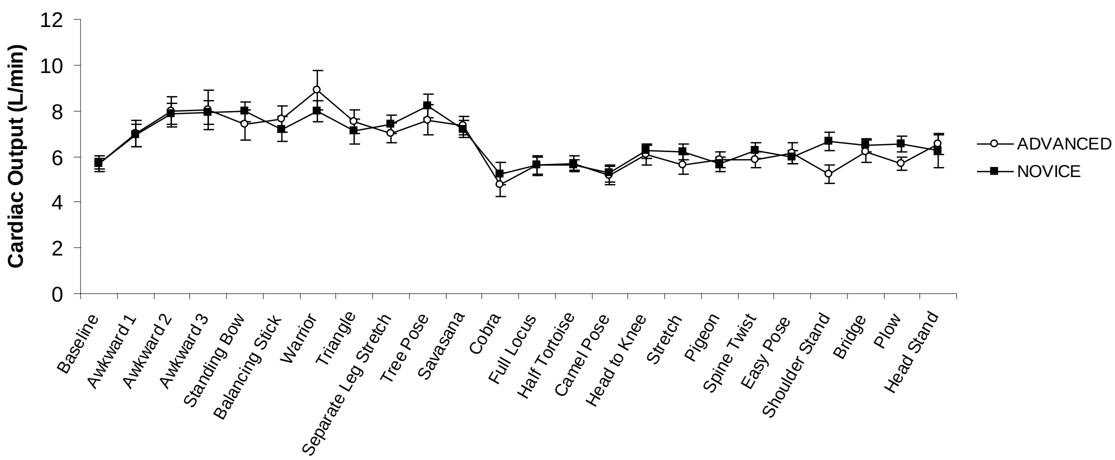

Diastolic Blood Pressure
120
100
80
60
40
20
0
Diastolic BP (mmHg)
ADVANCED
NOVICE
Baseline
Awkward 1
Awkward 2
Awkward 3
Standing Bow
Balancing Stick
Warrior
Triangle
Separate Leg Stretch
Tree Pose
Savasana
Cobra
Full Locus
Half Tortoise
Camel Pose
Head to Knee
Stretch
Pigeon
Spine Twist
Easy Pose
Shoulder Stand
Bridge
Plow
Head Stand

Appendix C

Stroke Volume



Cardiac Output

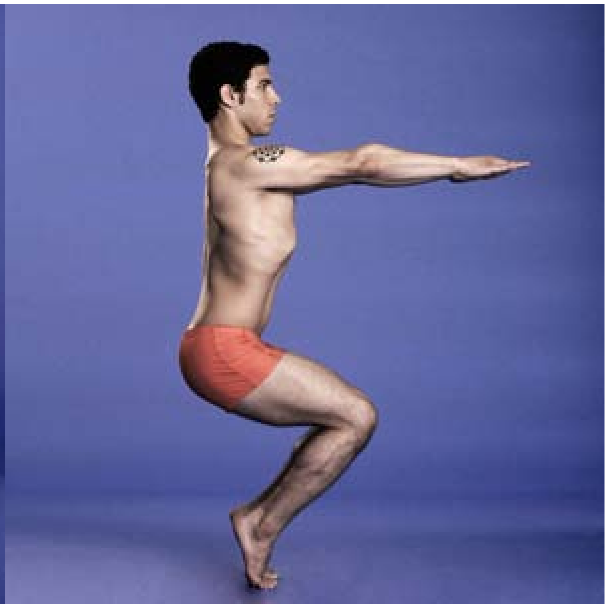


Appendix D

Pranayama (Deep breathing)

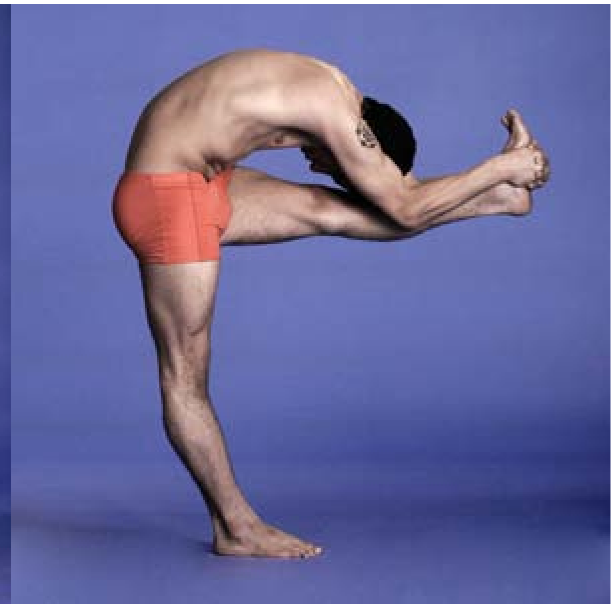
Half Moon Pose

Hands to Feet Pose

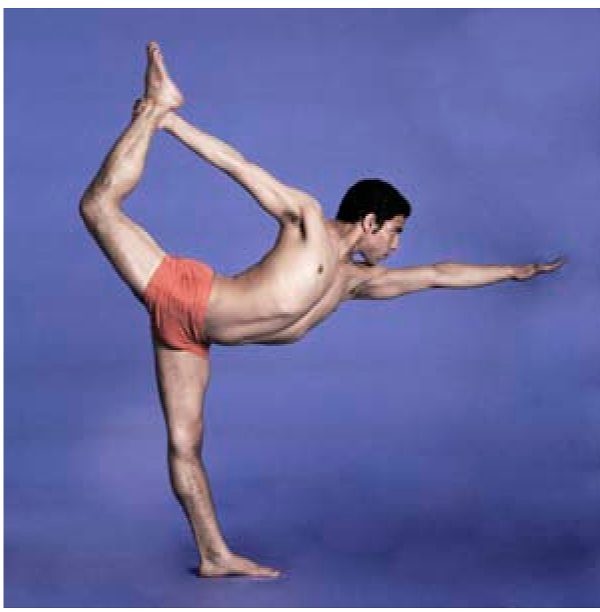


Awkward Pose

Eagle Pose



Standing Head to Knee



Standing Bow Pose

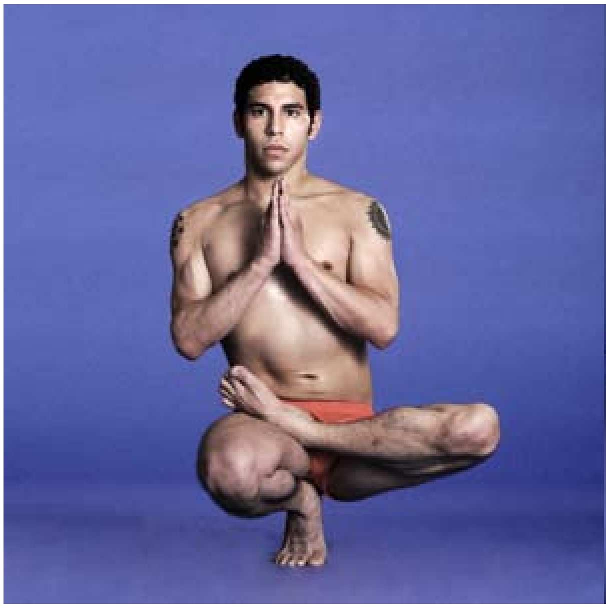
Balancing Stick

Standing Separate Leg Stretching Pose

Triangle Pose

Standing Separate Leg Head to Knee Pose

Tree Pose



Toe Stand

Corpse Pose (Savasana)

Wind-Removing Pose

Cobra Pose

Locust Pose

Full Locust Pose

Bow Pose

Fixed Firm Pose

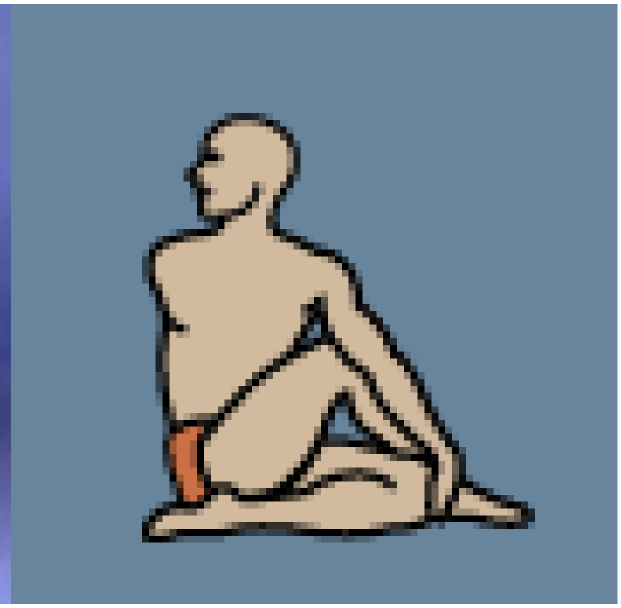
Half Tortoise Pose

Camel Pose

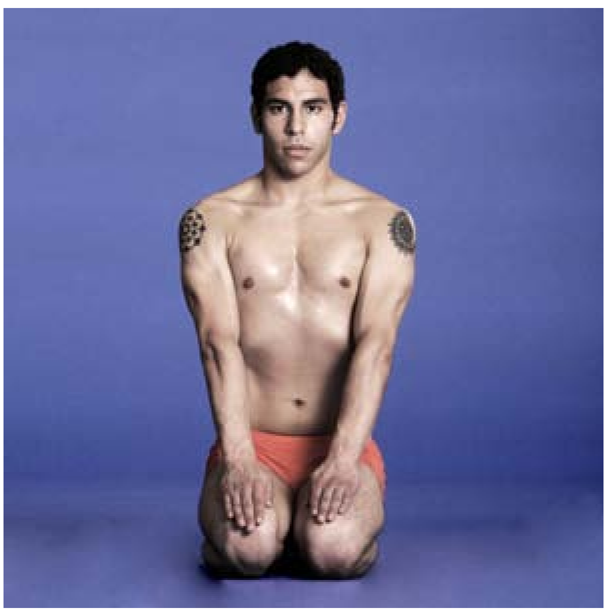
Rabbit Pose

Head to Knee Pose

Stretching



Spine-Twisting Pose



Blowing in Firm Pose

http://www.yogadallas.com/site/page/pg3472.html

Appendix E

Research Health Questionnaire

Cardiovascular Aging Research Laboratory

Personal Information

Today's Date ______________ Subject ID __________________________

Date of Birth ____________ Age ______ Sex ☐ Male
☐ Female: Date of Last Menstrual Period:________

Please circle the highest grade in school you have completed:

Elementary school	1	2	3	4	5	6	7	8
High school	9	10	11	12				
College/Post Grad	13	14	15	16	17	18	19	20+

What is your marital status? ☐ Never Married ☐ Married ☐ Widowed ☐ Divorced; Separated

Ethnic Background: ☐ Hispanic or Latino ☐ Not Hispanic or Latino

Race:

☐ White ☐ American Indian/Alaskan Native ☐ Pacific Islander

☐ Black or African American ☐ Asian ☐ Other: ____________________________

Symptoms or Signs Suggestive of Disease

Check appropriate box:

Yes	**No**		
☐	☐	1.	Have you experienced unusual pain or discomfort in your check, neck, jaw, arms or other areas that may be due to heart problems?
☐	☐	2.	Have you experienced unusual fatigue or shortness of breath at rest, during usual activities, or during mild-to-moderate exercise (e.g., climbing stairs, carrying groceries, brisk walking, cycling)?
☐	☐	3.	When you stand up, or sometimes during the night while you are sleeping, do you have difficulty breathing?
☐	☐	4.	Do you lose your balance because of dizziness or do you ever lose consciousness?
☐	☐	5.	Do you suffer from swelling of the ankles (ankle edema)?
☐	☐	6.	Have you experienced an unusual and rapid throbbing or fluttering of the heart?
☐	☐	7.	Have you experienced severe pain in your leg muscles during walking?
☐	☐	8.	Has a doctor told you that you have a heart murmur?

Chronic Disease Risk Factors

Check appropriate box:

Yes	No		
☐	☐	9a.	Are you a male over age 45 years or a female over age 55 years?
☐	☐		b. Are you a female who has experienced premature menopause?
☐	☐		c. If you answered “yes” to 9b, are you on estrogen replacement therapy?
☐	☐	10.	Has your father or brother had a heart attack or died suddenly of heart disease before the age of 55; has your mother or sister experienced these heart problems before the age of 65?
☐	☐	11.	Are you a current cigarette smoker? If quit smoking, when? Date:

Yes	No		
☐	☐	12.	Has a doctor told you that you have high blood pressure (more than 140/90 mm Hg) or a heart condition?
☐	☐	13.	Is your total serum cholesterol greater than 200 mg/dl, or has a doctor told you that your cholesterol is at a high risk-level?
☐	☐	14.	Do you have diabetes mellitus?
☐	☐	15.	Are you physically inactive and sedentary (little physical activity on the job or during leisure time)?
☐	☐	16.	Do you have a bone or joint problem that could be made worse by a change in your physical activity?
☐	☐	17.	During the past year, would you say that you have experienced enough stress, strain, and pressure to have a significant effect on your health?
☐	☐	18.	Do you eat foods nearly every day that are high in fat and cholesterol such as fatty meats, cheese, fried foods, butter, whole milk, or eggs?
☐	☐	19.	Do you weigh 30 or more pounds than you should?
☐	☐	20.	Do you know of any other reason you should not do physical activity?

Medical History

21. *Please check which of the following conditions you have had or now have. Also check medical conditions in your family (father, mother, brother(s), or sister(s)). Check as many as apply.*

Self	Family	Medical Condition	Self	Family	Medical Condition
☐	☐	Coronary heart disease, heart attack; by-pass surgery	☐	☐	Major injury/fracture to foot, leg, knee
☐	☐	Arrhythmias	☐	☐	Major injury to back or neck
☐	☐	Angina	☐	☐	Major injury/fracture to hip or shoulder
☐	☐	Marfan’s syndrome			
☐	☐	High blood pressure	☐	☐	Recent leg trauma/injury
☐	☐	Peripheral vascular disease	☐	☐	Rheumatoid arthritis
☐	☐	Phlebitis or emboli	☐	☐	Osteoarthritis
☐	☐	Other heart problems	☐	☐	Osteoporosis
☐	☐	Stroke	☐	☐	Fibromyalgia

Self	Family	Medical Condition	Self	Family	Medical Condition
☐	☐	Asthma	☐	☐	Chronic fatigue syndrome
☐	☐	Bronchitis	☐	☐	Systemic lupus erythematosus
☐	☐	C.O.P.D. (emphysema)	☐	☐	Anemia (low iron)
☐	☐	Pulmonary embolism (blood clots in lungs)	☐	☐	Thyroid problems
			☐	☐	Gout
☐	☐	Deep vein thrombosis (blood clots in legs)	☐	☐	Kidney disease
			☐	☐	Nephrotic syndrome
☐	☐	Antithrombin III deficiency	☐	☐	Gallstones/gallbladder disease
☐	☐	Inherited hypercoaguability	☐	☐	Liver disease (cirrhosis)
☐	☐	Acquired hypercoaguability	☐	☐	Hepatitis
☐	☐	Factor V leiden mutations	☐	☐	Diabetes mellitus
☐	☐	Protein C deficiency	☐	☐	Raynaud's disease
☐	☐	Protein S deficiency	☐	☐	Crohn's disease
Self	**Family**	**Medical Condition**	**Self**	**Family**	**Medical Condition**
☐	☐	Stomach/duodenal ulcer	☐	☐	Hysterectomy
☐	☐	Rectal growth or bleeding	☐	☐	Problems with menstruation
☐	☐	Irritable bowel syndrome	☐	☐	Post-menopausal
☐	☐	Lung cancer			Date:
☐	☐	Breast cancer	☐	☐	Allergies
☐	☐	Prostate cancer	☐	☐	Depression
☐	☐	Skin cancer	☐	☐	Anxiety, phobias
☐	☐	Colorectal cancer	☐	☐	Eating disorders
☐	☐	Other cancer Specify:	☐	☐	Substance abuse problems (alcohol, other drugs, etc.)
☐	☐	Hearing loss	☐	☐	Sleeping problems
☐	☐	Cataracts	☐	☐	Other
☐	☐	Glaucoma			Specify:

Please specify and include information on any recent illnesses, hospitalizations, surgical procedures, or other health problems.

____
____
____

22a. Are you currently pregnant, think you may be pregnant, or are currently trying to get pregnant?

☐ Yes ☐ No ☐ Not sure ☐ Not applicable (male or post-menopausal)

b. If you answered "yes" or "not sure" to 22a, do you need a pregnancy test? ☐ Yes ☐ No

23. Do you currently have or have you had an infection within the last 4 weeks?

☐ Yes ☐ No

24. *Please check any of the following medications you take regularly and give the name and dose of the medication.*

Medication	**Name of Medication**
☐ Heart medicine	______________________
☐ Blood pressure medicine	______________________
☐ Blood cholesterol medicine	______________________
☐ Thromboembolic disease medicine	______________________
☐ Hypercoaguability medicine	______________________
☐ Steroids	______________________
☐ Hormones/HRT	______________________
☐ Birth control medicine	______________________
☐ Medicine for breathing/lungs	______________________
☐ Insulin	______________________
☐ Other medicine for diabetes	______________________
☐ Arthritis medicine	______________________
☐ Medicine for depression	______________________
☐ Medicine for anxiety	______________________
☐ Thyroid medicine	______________________
☐ Medicine for ulcers	______________________
☐ Painkiller medicine	______________________
☐ Allergy medicine	______________________
☐ Dietary supplements (herbs, vitamins, etc)	______________________
☐ Other (please specify)	______________________

25. Do you have any known drug allergies? ______________________

Body Weight

26. What is the most you have ever weighed? _______________

27. Are you now trying to:

☐ Lose weight ☐ Gain weight ☐ Stay about the same ☐ Not trying to do anything

Stress

28. During the past month, how would you rate your overall level of stress?

☐ Very high ☐ High ☐ Moderate ☐ Low

29. In the past year, how much effect has stress had on your health?

☐ A lot ☐ Some ☐ Hardly any or none

30. On average, how many hours of sleep do you get in a 24-hour period?

☐ Less than 5 ☐ 5-6 ☐ 7-9 ☐ More than 9

Substance Use

31. How would you describe your cigarette smoking habits?

☐ Never smoked

☐ Used to smoke. How many years or months has it been since you smoked? _______ years/months (circle one)

☐ Still smoke. How many cigarettes a day do you smoke on average? _____ cigarettes/day

32. How many alcoholic drinks do you consume? (A “drink” is a glass of wine, a wine cooler, a 16oz bottle/12oz can of beer, a shot glass of liquor, or a mixed drink).

☐ Never use alcohol ☐ Less than 1 per week ☐ 1-6 per week
☐ 1 per day ☐ 2-3 per day ☐ More than 3 per day

33. In one sitting, how many drinks do you typically consume? ____________________
34. How many cups (8 ounces) of coffee do you drink per day? ____________________
35. How many ounces of sodas containing caffeine do you drink per day? ____________

Physical Fitness, Physical Activity/Exercise

36. Considering a **7-Day period** (a week), how many times on the average do you do the following kinds of exercise for **more than 15 minutes** during your **free time** (write on each line the appropriate number)?

a) **STRENUOUS EXERCISE (HEART BEATS RAPIDLY)** **Times Per Week**
(i.e. running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling) ____________

b) **MODERATE EXERCISE (NOT EXHAUSTING)**
(i.e. fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing) ____________

c) **MILD EXERCISE (MINIMAL EFFORT)**
(i.e. yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking) ____________

37. Considering a 7-Day period (a week), during your leisure-time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?

☐ OFTEN ☐ SOMETIMES ☐ NEVER/RARELY

38. How long have you exercised or played sports regularly?
☐ I do not exercise regularly ☐ Less than 1 year ☐ 1-2 years
☐ 2-5 years ☐ 5-10 years ☐ More than 10 years

39. If you do not exercise regularly, have you been inactive for at least 6 months?
☐ Yes ☐ No

40. Please describe your regular physical activity during a typical week. Please include the intensity, duration, and type of activity. If you do not exercise, write “none”.

	Activity	Duration (time)	Intensity
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Occupational Health

41. Please describe your main job title and duties.

---

42. How much hard physical work is required on your job?

☐ A great deal ☐ A moderate amount ☐ A little ☐ None

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Vita

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